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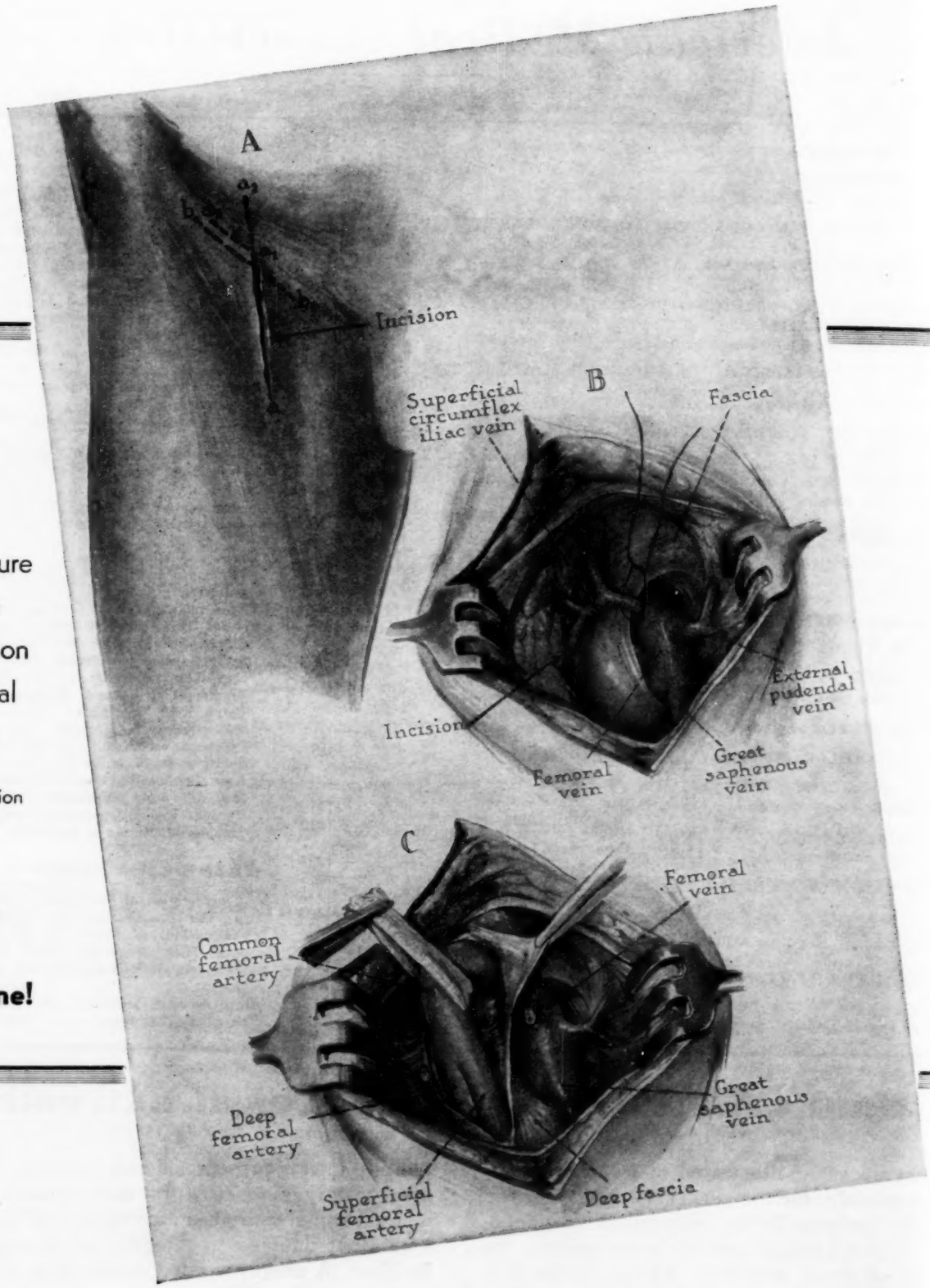

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CARCINOMA OF THE STOMACH

NECESSITY FOR REEVALUATION OF THERAPEUTIC PHILOSOPHY

Alton Ochsner, M.D.
and
John Blalock, M.D., New Orleans

Since the earliest medical writings, cancer of the stomach has been a common lesion, and it still remains one of the most frequently occurring malignant tumors in men. In 1948, there were 26,219 deaths from cancer of the stomach reported in the United States. Lawton and co-workers [1] state that during World War II, over 300,000 men were killed in action and about the same number of persons were killed in the United States by cancer of the digestive tract. One-third of these, or 100,000 deaths, were due to cancer of the stomach, and they estimate that within 10 years deaths from cancer of the stomach will exceed 40,000 annually.

Berkson and co-workers [2] state that 10% of persons admitted to the Mayo Clinic had a malignant neoplasm and in 1 of every 20 of these the neoplasm was located within the stomach. In other words, 1 in every 200 patients admitted to the Mayo Clinic had gastric cancer. Almost identical figures are reported by Lawton and associates.[1] In their series of 170,962 patients admitted to Hines Hospital, 21,160 patients had cancer, and in 1,004 of these the lesion was located in the stomach; in other words, 0.6% of the total patients admitted and 4.7% of the cancer patients had gastric malignant lesions.

The incidence of gastric carcinoma in the South is lower than in other parts of the country, except among Negroes. In New Orleans, in 1947, the number of cases of gastric cancer per 100,000 population was 23.5 for white persons and 36.6 for Negroes.[3] For that year the total incidences in San Francisco and Alameda counties and in Denver were 30.6 and 26.9, respectively.[3] From 1941 to 1951, inclusive, 587,356 patients were admitted to Charity Hospital in New Orleans, of which 2,211 had gastric carcinoma, an incidence of 0.376% or 1 in every 265 admissions.[4] The incidence of gastric cancer among all patients admitted was 0.358% (1 in 279) for white patients and 0.387% (1 in 258) for Negroes. If the obstetric patients are excluded, these incidences are 0.397 (1 in 277) in white persons and 0.507 (1 in 197) in Negroes. In the Ochsner Clinic, the percentage of gastric malignant lesions among patients admitted was 0.18, or 1 in every 555 patients. The respective incidence for gastric carcinoma, excluding other gastric malignant neoplasms, was 0.17%, or 1 in every 588 patients admitted.

Despite the frequency of cancer of the stomach and the fact that it has been a common lesion for a long time, the results obtained from its treatment have been far from satisfactory. There is a great deal of variation in the operability and resectability incidences in gastric carcinoma, varying from an operability rate of 88.9% reported by Bocharov,[5] 86% by Winkelbauer,[6] 80.8% by Rhoads,[7] and 80.9% by Maimon and Palmer [8] to a low operability rate of 50% reported by Allen [9] and Clark.[10] In our series, 76.6% were operated on. When it is considered that these statistics are based on the study of patients admitted to large institutions and that many patients with gastric cancer do not get to the hospital, the relatively low operability incidence becomes even more apparent. Clark [10] showed that of all the reported cases of gastric cancer in a large metropolitan area (Houston, Texas) only 30% were operable. The resectability incidence varies considerably from a high of 54% reported by Winkelbauer [6] to 30% reported by Lawton,[1] 35% by Pack,[11] and 25% by Clark.[10] In our series, only 33.3% were resectable. Clark's study [10] further showed that of all cases in a metropolitan area, only 5.7% were resectable. The five year survival rates among all patients admitted to the various institutions varies considerably, but it is tragically low, ranging from about 5% (Clark [10] 5%, Lawton [1] 5%, State [12] 6.6%, and Welch and Allen [13] 7%) to 14% (Berkson and co-workers [2]). In all the cases in a metropolitan area reported by Clark, the five year survival rate was 0.8%. In our series, the five year survival rate was about 10%. It is, indeed, a sad

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commentary that in a condition as common as gastric carcinoma such poor therapeutic results have been obtained, and, because of this, it appears that a reevaluation of the therapeutic philosophy in gastric cancer is necessary.

CHOICE OF THERAPY

Because it has been frequently observed that, following subtotal gastric resection for carcinoma, recurrence occurs in the remaining gastric pouch, it has been suggested that more radical procedures be done. Walters, Gray, and Priestley [14] found that in 40 of 120 cases of cancer of the stomach death occurred as the result of recurrence in and about the stomach. Stout [15] reported eight cases in which autopsies were done six months or more after subtotal gastrectomy in all of which death was due to cancer. In one, a new and independent cancer had developed in the gastric remnant 23 years after resection; three patients died of widespread metastasis with no local neoplasm, but three died of local recurrence with no metastases. McNeer and co-workers,[16] in an autopsy series of 92 patients who had had gastrectomies for gastric carcinoma, found that in 46 (50%) there was local recurrence of carcinoma either at the gastroenterostomy site or in the wall of the stomach, within varying periods from 2 to 75 months after the gastrectomy. There was failure to control the lesion in 74 (80.4%) of the 92 cases, with 46 (50%) recurrences in the gastric remnant, 9 (9.8%) in the duodenal stump, and 19 (20.7%) in the perigastric nodes and gastric bed.

Whereas previously it was thought that the duodenum was relatively immune to involvement from gastric carcinoma, it has been shown that such is not the case, and it is essential in doing a gastrectomy to remove at least the first portion of the duodenum. Coller and associates [17] found, in careful microscopic examination of the removed specimen following gastrectomy for carcinoma, that the duodenum was involved in 26.4% of the patients. McNeer and associates,[16] in a study of a series of patients who had been subjected to gastrectomy and subsequently to autopsy found involvement of the duodenal stump in 9.8%. Berne and Freedman [18] found the duodenal stump involved in 7%. Borrmann [19] found it involved in 20 of 69 cases of gastric carcinoma, and Konjetzny [20] in 67% of cases in his series. Harvey and co-workers [21] found that, in a series of 270 cases in which resection was done, the duodenum was involved in 53 and the esophagus in 37. More than one-fourth of the antral tumors invaded the duodenum. Castleman [22] found that carcinoma of the distal end of the stomach frequently involved the duodenum but rarely extended beyond 1 cm.

Because of the local recurrence in the remaining stump of the stomach and the relatively low five year salvage rate following partial or so-called subtotal gastrectomy, many workers have advocated total gastrectomy to improve the results. Allison [23] has described such a procedure: "A block dissection has been performed to include the whole of the stomach, the lower end of the esophagus, the greater omentum, the lesser omentum flush with the liver and medially up to the hepatic artery, the spleen, the pancreas with retroperitoneal tissue and glands as far as the neck, the left gastric vessels and surrounding tissue as far back as the celiac axis, a cuff of diaphragm around the cardia and the posterior mediastinal cellular tissues as high as the inferior pulmonary vein. The duodenum is closed and the esophagus is anastomosed to the jejunum." McNeer and co-workers [24] report a series of cases in which metastasis occurred in the remaining portion of the stomach following "subtotal" gastrectomy. Ranson [25] reports special studies made of tissues taken from the upper and lower ends of the operative specimens in 44 of 60 cases of total gastrectomy. There was evidence of extension to the esophageal line of the resection in 21 patients and similar extension to the duodenal end in 13. Because of possible extension beyond the line of resection McNeer and associates [24] advocate removing a circumferential section of the specimen at the line of resection, which is submitted to examination by frozen section at the time of the operation. The proponents of total gastrectomy for all gastric carcinomas are numerous.[26]

Although it is incriminating that local recurrence should occur in the remaining gastric pouch following gastrectomy for cancer of the stomach, one must be sure about the extent of the resection before one concludes that total gastrectomy would have prevented the recurrence. McNeer and associates [16] showed that in 60 cases at the Memorial Hospital in which it was possible to determine the extent of resection, there was no local recurrence in 16 and local recurrence in 44. Of the 16 with no local recurrence, 4 (25%) had less than 25% of the stomach resected, 4 (25%) had one-half resected, 7 (43.8%) had from one-half to three-fourths resected, and only 1 (6.3%) had more than three-fourths of the stomach resected. Of the 44 with local recurrence, 7 (15.9%) had less than one-fourth of the stomach resected, 15 (34.1%) had one-half resected, 20 (45.5%) had from one-half to three-fourths resected, and only 2 (4.5%) had more than three-fourths resected. It is interesting that only 3 of the 60 patients had more than 75% of the stomach removed. It is obvious, therefore, that when one speaks of a gastric resection that is anything less than total resection, one must define what is meant by such a resection.

Unfortunately, too often incomplete resection for gastric cancer is performed, as evidenced by the experience of McNeer and associates [24] at Memorial Hospital. In fact, we have seen a number of patients in whom such a small amount of stomach was removed that the operation might justifiably be termed a biopsy rather than a resection. In too few publications concerning the treatment of gastric cancer is the extent of the gastric resection designated. Unfortunately, almost any type of gastric resection is frequently described as subtotal resection, whereas subtotal gastric resection should imply radical removal of all except an extremely small portion of the stomach. Because of the confusion that exists in the literature about gastric resections, we have designated such a resection as a "radical subtotal resection" in contradistinction to the much less complete operation that is frequently described as subtotal resection.

By radical subtotal gastric resection we mean removal of all the first portion of the duodenum and all the lesser curvature up to the cardia; removal of all the

greater curvature up to within 5 or 6 cm. of the cardia; removal of all the gastrohepatic omentum, the gastrocolic omentum, and the greater omentum; careful dissection of and removal of the lymph nodes along the lesser curvature, especially those around the celiac axis and the left gastric vessels, the subpyloric nodes, the subhepatic nodes, the gastrolineal nodes, and the paraesophageal nodes. We do not believe that the radical procedure described by Allison [23] is generally practical. Although it may be necessary to do as radical a procedure as Allison suggests in certain cases, it is our belief that in many patients in whom the lesion is located in the distal end of the stomach, no more can be accomplished than is accomplished by a radical subtotal resection of the type described above. Walters [27] states that although there is an increased number of total gastrectomies performed at the Mayo Clinic because the operation has become relatively safe, he believes subtotal resection will give as good or better results than total resection, with a considerably lower mortality. Fletcher [28] also believes that there is insufficient evidence at present to warrant the general adoption of total gastrectomy for all gastric cancers. Templeton and associates [29] are of the same opinion. ReMine and Priestley [30] state, "This suggests that if the growth is in the distal portion of the stomach, complete removal of the stomach offers no more chance for long survival than if an adequate subtotal gastric resection is performed."

It should be emphasized that we are not opposed to total gastrectomy for gastric carcinoma; in fact, we believe that this is the procedure of choice when the lesion is located in the proximal portions of the stomach and in all cases in which the lesion can be completely removed only by total resection. On the other hand, we believe that most lesions located in the pyloric end of the stomach can be treated just as radically by radical subtotal resection as by total resection. Although it may seem inconsequential to quibble whether all of the stomach or all except an extremely small portion should be removed, we are convinced from our experience that

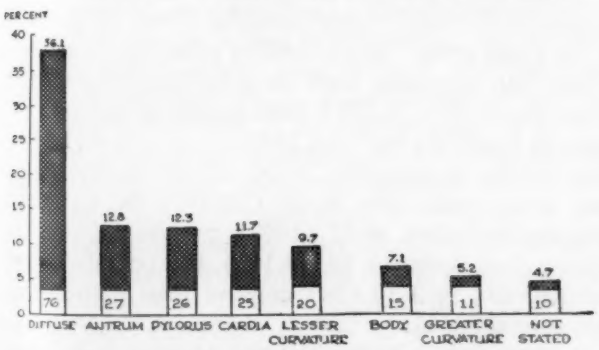

Fig. 1.—Location of malignant lesion in 210 cases of gastric carcinoma.

the small gastric pouch, which is usually no larger than a man's thumb, makes the difference between the patient's being able to get along well with few or no digestive disturbances and becoming, as often occurs, a gastric cripple. Whether it is the remaining gastric pouch that is responsible for the paucity of symptoms following a radical subtotal resection cannot be stated with certainty. We are of the opinion that it is probably not the pouch that is responsible but rather the fact that some of the left vagus fibers are intact in the radical subtotal resection, whereas in total resection both vagi are completely interrupted.

TYPE AND LOCATION OF TUMORS IN PRESENT STUDY

The present report is based on an analysis of 220 cases of primary gastric malignant lesions observed in the Ochsner Clinic in the 10 year period from January,

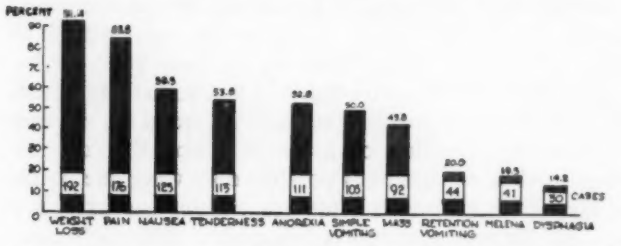

Fig. 2.—Frequency of occurrence of various signs and symptoms of gastric carcinoma in 210 patients.

1942, to January, 1952. Of these, 210 (95.4%) were carcinoma, 5 (2.2%) were leiomyosarcoma, 3 (1.2%) were reticulum cell sarcoma, and 1 each (0.5%) were lymphosarcoma and Hodgkin's disease. One hundred and fifty-four (70%) patients were men and 66 (30%) were women. The average age for the men was 57.5 years and for the women, 55.3 years.

The location of the tumor in the 210 patients with gastric carcinoma, as determined by the roentgenologist, was as follows: extensive and diffuse in 36.1% (76 patients); located primarily in the antrum in 12.8% (27 patients), in the pyloris in 12.3%, in the cardia in 11.7%, in the lesser curvature in 9.7%, in the body in 7.1%, and in the greater curvature in 5.2%; the location was not stated in 4.7% (fig. 1). The lesions were described by the pathologist as follows in 202 cases examined: in 133 (65.8%) there was diffuse involvement of the stomach, in 48 (23.8%) the lesion was ulcerative, and in 21 (10.4%) it was polypoid. Ragins and Cohen,[31] in 222 gastric resections for carcinoma, found that the lesion was of the diffuse, infiltrating type in 162 and polypoid in 17; the others were not described. Collins and Gall [32] believe that gastric cancer often occurs as a multicentric lesion. They found multiple independent malignant lesions in 26 of 117 resected stomachs.

SYMPTOMS

Unfortunately, gastric cancer in its incipiency produces few or no manifestations. It is our belief that too much emphasis has been placed on the so-called classical picture of gastric cancer, which usually, with few exceptions, is the picture of advanced disease. In the present series of 210 patients with gastric cancer there was an average duration of symptoms of 7.8 months and an average weight loss of 24.9 lb. (11.26 kg.) (fig. 2). Weight loss was the most prominent manifestation, being present in 91.4% of the patients; pain occurred in 83.8%, nausea in 59.5%, tenderness in 53.8%, anorexia in 52.8%, simple vomiting in 50%, palpable mass in 43.8%, retention vomiting in 20%, melena in 19.5%, and dysphagia in 14.2%. Lawton and associates [1] stated that 56% of their patients had, as early complaints, loss of appetite, fulness, and indiges-

tion. In all their cases an average of 19 months elapsed between the onset of the first symptom and admission of the patient to the hospital.

DIAGNOSIS

It is generally thought that the diagnosis of gastric carcinoma is relatively simple, and, of the various diagnostic procedures, roentgen examination of the stomach is thought to be most valuable. In the present series, roentgenologic diagnosis of gastric carcinoma was made in 96.5% of the cases; the diagnosis was missed in only 3.5%. A correct diagnosis in over 96% of instances is an excellent record. Yet it is something which we wish were not possible, because we are of the opinion that the visualization of a gastric lesion that can be diagnosed as carcinoma is possible only when the lesion is far advanced and, all too frequently, has extended beyond the stomach and is inoperable. Although mass roentgenography has been used as a screening technique for gastric carcinoma, it has not proved satisfactory and has not been productive of sufficient correct diagnoses to justify its being used. Roach and coworkers [38] found in a recent mass roentgen survey that asymptomatic cancer or its precursors was found in only one in every 476 examinations. We hope that in the not too distant future it will be possible to diagnose with a high degree of accuracy, most cases of gastric carcinoma before they are large enough to be visualized roentgenographically.

TREATMENT

Of the 210 cases of gastric carcinoma included in the present series, 27 (12.8%) were so far advanced when first seen that they were considered inoperable, and the patients were treated by nonoperative palliative measures. In 183 patients (87.2%) it was considered operable; 15 (7%) of these refused surgery or returned home to be operated on. One hundred sixty-eight (80%) of the entire group were explored; in 98 (46.6%) the lesion was found to be nonresectable. Of the 98 in whom exploration alone was done, 14 (14.2%) died in the hospital and 84 (85.8%) left the

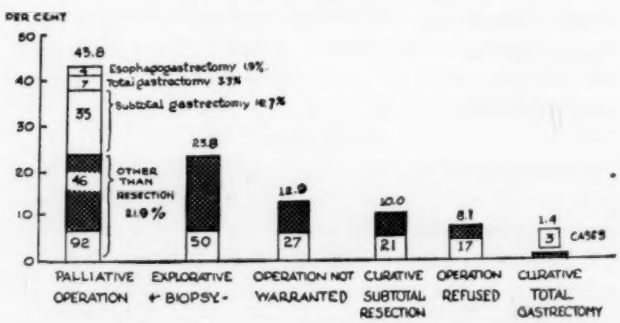

Fig. 3.—Method of treatment in 210 cases of gastric carcinoma.

hospital. In 70 patients (33.7% of the entire group) a resection was done, and in 46 (65%) of these it was termed a palliative resection. In contradistinction to our previous reports, cases of palliative resection in this report include all cases in which there was either gross or microscopic extension beyond the stomach. Previously, we considered as palliative procedures cases in which there was extension beyond the stomach or regional lymph nodes. Of the 46 patients in whom palliative resection was done, 35 (76%) had subtotal gastrectomy, of whom 5.7% died in the hospital and 94.3% left the hospital. Four (8%) patients had esophagogastrectomy for extensive disease, two of whom died in the hospital. Seven (15.2%) patients had total gastrectomy, three of whom died in the hospital. The high mortality rate in patients with esophagogastrectomy and

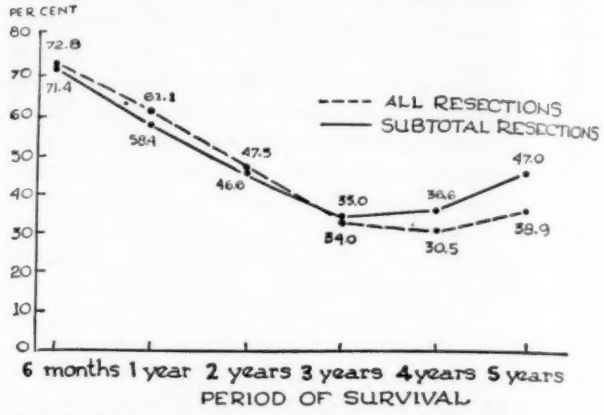

Fig. 4.—Comparison between survival rates for patients treated by subtotal gastric resection and those for the entire group.

total gastrectomy was due to the extent of the disease and not to the operative procedure. In 24 patients the resection was considered curative, because there was neither gross nor microscopic evidence of extension beyond the stomach. That not all of them were cured is shown by the subsequent statistics, illustrating that even the absence of microscopic evidence of extension beyond the stomach does not necessarily mean all of the tumor has been removed. Twenty-one (87.5%) of these 24 were treated by subtotal resection. Two (9.5%) died in the hospital, and 19 (90.5%) left the hospital. Three (12.5%) of the 24 in whom a curative resection was done had total resection and all survived.

Of the entire group of 210 patients, 92 (43.8%) had some type of palliative procedure, of whom 46 (21.9% of the entire group) were treated by palliative procedures other than resection, such as gastrojejunostomy and jejunostomy, 35 (16.7%) were treated by subtotal resection, 7 (3.3%) had total gastrectomy, and 4 (1.9%) had esophagogastrectomy. In 50 (23.8%) exploration and biopsy were done, in 27 (12.9%) the operation was not warranted, in 21 (10%) curative subtotal resection was done, in 17 (8.1%) the operation was refused, and in 3 (1.4%) curative total gastrectomy was done (fig. 3).

To recapitulate, of the 210 patients with gastric carcinoma, 92 (43.8%) had palliative procedures, 50 (23.8%) had exploration and biopsy, in 44 (21%) the operation was not warranted or was refused, and in only 24 (11.4%) of the entire group was a curative resection possible. The hospital mortality rate according to the type of procedure was as follows: esophagogastrectomy 50%, total gastrectomy 30%, palliative procedures other than gastrectomy 16.2%, exploration only 13.4%, curative subtotal resection 9.5%, and palliative subtotal resection 7.9%.

SURVIVAL RATES

In the consideration of the results obtained with any form of therapy, long-term survival rates are important. In determining these rates, we have assumed that any patient not surviving a given period died because of this disease. Obviously, this gives a poorer outlook, but we believe it is justifiable, because the personal equation cannot enter into the calculation. In determining the survival rates at various periods, the percentage of patients surviving for each time interval stated was based on the number of patients operated on at the beginning of that interval (fig. 4, 5, and 6). Of the group of patients in whom no resection was done, who had, obviously, the most advanced cases, 14.4% were alive at the end of six months, 4.03% were alive at the end of one year, and only one in a group of 109 (0.9%) was alive at the end of two years. No patient lived three years. In the group of patients in whom some type of resection was done, 72.8% were alive at the end of six months, 61.1% at the end of a year, 47.5% at the end of two years, 38.9% at the end of five years. In the cases in which radical subtotal resection was done, the survival rates are almost identical: 71.4% survived six months, 58.4% one year, 46.6% two years,

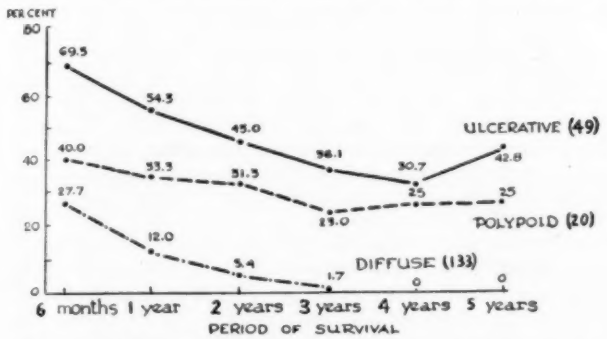

Fig. 5.—Survival rates according to type of malignant lesion found in 202 patients with gastric carcinoma.

and 47% five years. Actually, the five year survival rate in the subtotal resection group was slightly higher than in the total group who had resections (fig. 4). Subtotal resection gave results as good or better than those obtained in the entire group. Palliative radical subtotal resections (those done in patients in whom there was either gross or microscopic evidence of spread beyond the stomach) gave satisfactory results: 68.5% survived six months, 47% one year, 34% two years, and 20% five years. On the other hand, in the curative subtotal resections in which there was no gross or microscopic evidence of extension beyond the stomach, the results were excellent: 85.7% survived six months, 89.4% one year, 81.2% two years, and 85.7% five years.

There was considerable variation in the length of survival according to the type of lesion (fig. 5). Patients with diffuse lesions survived the shortest period, which might be expected because they had more extensive disease. Of this group, 27.7% survived six months, 12% one year, 5.4% two years, and only 1.7% three years. No patient lived as long as four years. Polypoid lesions gave better results: 40% survived six months, one-third survived two years, and one-fourth survived five years. The ulcerative lesions gave the best results: 69.3% survived six months, 54.3% one year, 45% two years, and 42.8% five years. Pack and McNeer [34] found that of the patients with polypoid gastric cancer, 26.3% survived five years and of those with ulcerative lesions, 33.9%

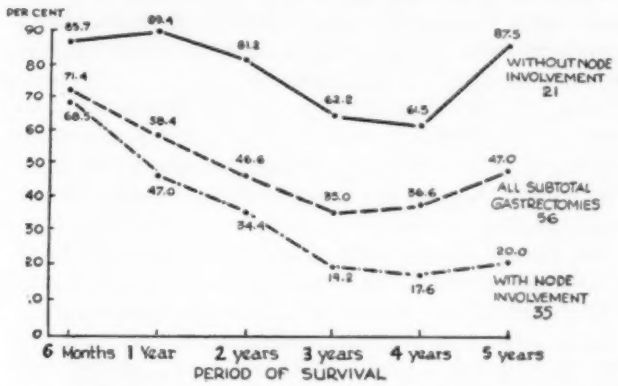

Fig. 6.—Comparison of survival rates between patients with and those without lymph node involvement, who were treated by subtotal gastric resection.

survived five years, whereas those with infiltrating tumors had the remarkably high 25% five year survival rate.

In addition to the type of lesion, survival rates vary with lymph node involvement. Whereas 47% of patients in whom radical subtotal resection was done survived five years, 20% of those with nodal involvement, and 87.5% of those without nodal involvement survived five years (fig. 6). Pack and McNeer,[34] in patients subjected to gastrectomy, obtained five year survival rates of 24.2% in those with nodal involvement and 42.8% in those without nodal involvement.

To summarize, in the present total series, exploration was done in 76.6% and resection in 33.3%. Twenty-nine per cent survived the resection, and 9.9% were alive at the end of five years (fig. 7).

RELATION OF TYPE OF THERAPY TO SURVIVAL RATE

It is indeed a sad commentary and a real indictment of the medical profession that a lesion as common and as well known as gastric carcinoma is treated so in-

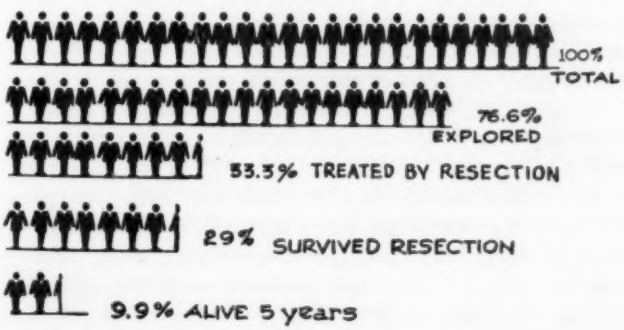

Fig. 7.—Management and results in 210 cases of gastric carcinoma.

adequately. The fact that only 10% of all patients seen are alive at the end of five years is indeed deplorable. As mentioned previously, many physicians advocate total gastrectomy in all cases of gastric cancer, regardless of their location and extent. This study shows, how-

ever, that radical subtotal gastrectomy, when it can be done, gives excellent results (47% five year survival). This compares favorably with the statistics reported by Berkson and associates [2] from the Mayo Clinic showing a 31.6% five year survival rate. On the other hand, Lampert and co-workers [35] reported a group of 73 patients from the Mayo Clinic in whom the clinical diagnosis was gastric ulcer or an ulcerating lesion of the stomach treated by gastrectomy, of whom 43.5% were alive at the end of five years. Obviously, since a preoperative diagnosis of gastric cancer was not made, the lesion was relatively early, and the results should have been better. A resection was possible for every patient in the group.

De Amesti,[26b] who is an ardent proponent of the use of total gastrectomy, reports only an 11% survival rate after this procedure. Lahey and Marshall [26e] report a five year survival rate of 9.4% following total gastrectomy for carcinoma in 127 cases. Of Pack and McNeer's [34] series of 16 patients who had total gastrectomy, 8 were alive at the end of five years. ReMine and Priestley [30] obtained a five year survival rate of 18% following total gastrectomy for gastric carcinoma. One of the survivors had lymphosarcoma, whereas the remainder had adenocarcinoma. Walters,[36] reporting the results following total gastrectomy for cancer of the stomach from the Mayo Clinic, states that 28.9% of his patients lived five years or longer and that if the lymph nodes were involved the five year survival rate was 16.5%, whereas if the lymph nodes were not involved it was 43.1%. It is obvious from these statistics that total gastrectomy will not increase the salvage rate in the treatment of gastric carcinoma. Since the more radical procedure, total gastrectomy, does not increase the five year survival rate, it must be concluded that better results will be obtained only when patients with gastric cancer are operated on earlier, at a time when the lesion is limited to the stomach.

DIAGNOSTIC DIFFICULTIES

It is generally thought that the diagnosis of gastric carcinoma is not difficult and that a positive diagnosis can be made in a high percentage of instances by means of fluoroscopy and roentgenography. In our own series, the roentgenographic diagnosis was correct in 96% of cases. Probably a diagnosis could be made in 100% of cases if there is enough delay to permit sufficient growth of the tumor so that it cannot be missed. Albot and Toulet [37] emphasize that in the early stages of gastric cancer, one is unable to differentiate between benign and malignant lesions of the stomach.

It is our conviction that if the results of treatment of gastric cancer are to be improved, treatment must be instituted at a time when the diagnosis cannot be made by the presently used diagnostic techniques. If one waits until the clinical picture and presently available laboratory examinations are positive, it is likely to be too late. For some time, one of us (A. O.) has emphasized to undergraduate students that, in order to increase the five year survival rate in gastric cancer, the patient must be treated when the disease cannot be diagnosed, that is, as gastric cancer. Although this philosophy may appear radical, something must be done to improve the results from the treatment of this common disease. Although some of the newer diagnostic techniques, such as cytological examinations of material obtained by the abrasive balloon suggested by Panico, Papanicolaou, and Cooper,[38] may increase the incidence of positive diagnoses, until they have been proved to be of statistical value, it is imperative that lesions that are not cancer clinically be removed and that the patient be treated as if he had cancer.

There are still many who believe that gastric ulcer should be treated conservatively and that it is similar to the lesion that occurs in the duodenum. In fact, at one time one of us (A. O.), too, was guilty of this misconception. Although peptic ulcer of the stomach does occur, it is our conviction that all gastric ulcers should be removed and none should be treated conservatively because of the inability to distinguish, in many instances, between benign and malignant ulcers. The roentgenologist is unable to determine whether an ulcer is benign or malignant and the gastroscopist is equally unable in many instances to differentiate malignant from benign ulcers, as is, also, the surgeon during the operation and even the pathologist when he examines the specimen in his hands. It is only after he has had a chance to examine the ulcer microscopically that the pathologist can determine whether it is malignant, and even then he may miss the diagnosis, as illustrated by the following case.

Mr. T. A. K., aged 44, was admitted to Foundation Hospital on Sept. 21, 1950, with the chief complaint of vomiting. He had had vague epigastric pain for about one year but had considered himself well until eight days prior to admission, at which time he experienced anorexia throughout the day, and in the evening nausea and cramping epigastric pain developed. He was awakened in the night by severe nausea, followed by vomiting, and shortly thereafter he passed a tarry stool. The following day he vomited on each attempt to eat, and during the subsequent two days he was able to retain only small amounts of liquids. His past history revealed no suggestion of peptic ulcer, except for the vague discomfort he experienced during the year. On examination, epigastric tenderness was the only abnormal finding.

Results of laboratory studies were entirely normal, including the blood cell count, erythrocyte sedimentation rate, and gastric analysis, which showed free hydrochloric acid of 60 degrees and total acid of 75 degrees. Roentgenographic studies of the upper gastrointestinal tract revealed alterations in the mucosal pattern in the distal one-third of the stomach, in some areas having the appearance of polyps. There was a constant defect having the appearance of an ulcer, and there was no evidence of obstruction at the time of this examination. The roentgenographic impression was that a malignant lesion of the stomach must be the first consideration.

The patient was operated on on Sept. 25, 1950. A mass was found in the posterior wall of the pyloric end of the stomach, which gave the gross impression of being a large ulcer, with possibly some polypoid excrescences around the periphery. Although the lesion did not appear to be malignant, it was thought best to treat it as such and, accordingly, the conventional radical subtotal gastrectomy was performed, with excision of all of the omentum, the gastrocolic omentum, and the gastrohepatic omentum, all of the lesser curvature of the stomach up to the cardia, and the greater curvature to within 6 cm. of the cardia. The subhepatic, celiac, left gastric, paraesophageal, gastrolineal, and subpyloric nodes were carefully dissected and removed. The duodenum was divided at the junction of the second and third portions. The duodenum was closed, and a retrocolic, isoperistaltic, short-loop, Hofmeister gastrojejunostomy was performed. Immediate examination by the pathologist resulted in the report of a benign gastric ulcer. The final study on the fixed specimen was again reported as benign gastric ulcer of the posterior wall of the greater curvature associated with profound chronic, inflammatory reaction

around the area of ulceration. The regional lymph nodes were identified and on examination were indicated to be hyperplastic only.

The patient's postoperative course was entirely uneventful, and he continued in good health until October, 1951, 13 months after the operation, when he noted a mass in the upper abdomen. Shortly thereafter pain occurred in the region of the mass and radiated to the region of the left costovertebral angle. Weight loss had been progressive despite a good appetite and what he considered to be an adequate intake. He was readmitted to the Foundation Hospital on Dec. 23, 1951. On examination, in addition to the epigastric mass, a 1.5 cm. left supraclavicular node, which was interpreted as Virchow's node, was found. An upper gastrointestinal series showed the anastomosis to be free. Excision biopsy of the supraclavicular node was performed, which revealed metastatic anaplastic carcinoma. Cachexia developed rapidly, and the patient died three months later.

Comment.—Although the histological diagnosis in this case was benign ulcer, although a radical subtotal gastric resection was done, and although no nodal involvement was found in the resected specimen, the patient succumbed to carcinoma. This obviously represents the exception, however.

According to Allen,[9] before 1939, 14% of his patients who were operated on for benign ulcer had cancer of the stomach. In more recent years, the incidence of error in diagnosis has been about 10%. He states that in the cases of gastrectomy in which the preoperative diagnosis is gastric ulcer, the chance of cure is twice as good as in the cases in which the preoperative diagnosis is cancer. Similar experience is reported by Comfort [39] from the Mayo Clinic. Engel [40] stated that the roentgenologist was unable to differentiate between benign and malignant ulcers in 34% of his cases. Lampert,[35] in a series of 550 cases of ulcers of the stomach that were diagnosed as benign at the Mayo Clinic, found that 73 (13%) were malignant. Although it was previously considered that benign gastric ulcers represented hazards because they were premalignant lesions, it is now generally accepted that an ulcerating lesion of the stomach is either primarily benign or primarily malignant and that, although the two may be confused, there is no causal relationship between the two. Allen [9] is convinced that benign ulcers do not become malignant. Brinton [41] suggested that chronic gastric ulcer could undergo a malignant change. The causal relationship between chronic gastric ulcer and gastric neoplasm was popularized, however, by Wilson and McCarty [42] in 1909, who, in a series of 153 cases of proved gastric carcinoma, found that 71% presented evidence of developing on the basis of preexisting ulcer. Stout [15] states that in 13.4% of 82 cases in which gastrectomy was done for cancer there was evidence that the cancer had developed at the margin of preexisting ulcers. He states that probably a larger percentage than this was actually preceded by ulcers, but since many of the cases were advanced, it was no longer possible to recognize the lesion as a peptic ulcer. He concludes: "Whatever one may believe about the relationship, it can be regarded as certain that whatever factors lead to the development of peptic ulcers are at least not unfavorable to the development of gastric cancer." Although it is probably impossible to state categorically that benign gastric ulcers do not become malignant, it is certainly not beyond the realm of possibility or even likelihood that a persistent lesion, such as an ulcer or even a scar resulting from the healing of an ulcer, in an epithelial membrane that is as susceptible to malignant change as is the gastric mucosa may be a premalignant lesion. It is well known that malignant change occurs in ulcers of the skin or even in the scars resulting from the healing of such ulcers (Marjolin's ulcer). Therefore, because of the impossibility of differentiating between benign and malignant ulcers by all of the presently available methods of diagnosis and also because of the possibility that an ulcer or a healed ulcer scar in the stomach may be a precancerous lesion, we are convinced that all gastric ulcers should be excised and that none should be treated conservatively.

Gastric polyps, which are definitely premalignant lesions, should also be treated radically. Kromer, Comfort, and But [43] found in a series of 195 cases of adenomatous gastric polyps that 35 (20%) were malignant. Certain cases of gastritis are premalignant lesions and must be removed. Stout [15] has observed in stomachs resected for cancer a patchy gastritis, which he describes as resembling the hyperplasia of mammary duct cells in the subclinical form of chronic cystic mastitis. He states "Stomachs with cancers in them not infrequently show this type of mucous membrane and there is some reason to believe that it may be regarded as a potential precancerous change." Konjetzny [20] was of the opinion that about 85% of gastric cancers developed on the basis of a chronic gastritis, which he thought was a precancerous condition. Orator [44] stated that about 80% of gastric carcinomas originate in chronic gastritis, which he designated as precancerous. Those conclusions were confirmed by Puchert.[45] Hurst [46] is also of the opinion that chronic gastritis is a precancerous lesion. On the other hand, Guiss and Stewart [47] believe that there is no causal relationship between gastritis and carcinoma of the stomach. Here again, it is our belief that a lesion that persists in a mucous membrane that is as susceptible to malignant change as gastric mucosa is a hazard and should be removed. All patients with chronic gastritis that does not respond to conservative measures should, therefore, be subjected to gastric resection.

Finally, if an increase in salvage rate is to be obtained, it is imperative that, occasionally, in patients whose clinical manifestations suggest cancer of the stomach but in whom no positive laboratory findings can be demonstrated, abdominal exploration be done to eliminate the possibility of a malignant lesion. If one waits until roentgenographic, gastroscopic, and cytological examinations are positive, the lesion will probably have extended to such a degree that nothing can be done curatively. Because carcinoma of the stomach begins so insidiously, it is imperative that in all men past 40 years of age who previously were well, who have not had dyspepsia, and in whom digestive disturbances develop for the first time that persist despite conservative therapy, exploratory laparotomy should be advised. Generally, the earliest manifestation is anorexia, severe enough to cause loss in weight. Although this will undoubtedly be regarded as an extremely radical philosophy, it is not as radical as it appears when one considers the extremely poor results that have been and still are being obtained in the treatment of gastric carcinoma. Although

one should not condone the performance of unnecessary operations, undoubtedly if one accepts the philosophy of operating for symptoms only in suspected carcinoma of the stomach, little is lost if, on exploration and careful examination of the stomach, nothing is found. On the other hand, if a lesion that could not be demonstrated by the usually employed laboratory techniques is found on abdominal exploration, radical subtotal resection will undoubtedly result in a cure. If the surgeon objects to operating on the basis of symptoms alone and waits until results of laboratory studies are positive, it is likely to be too late. That progress is being made in the treatment of gastric cancer is evidenced by the report of Berkson and co-workers,[2] in which it was shown that the operability rate in the Mayo Clinic increased 33% in the period 1940 to 1949 over the period 1907 to 1916. The resectability rate increased 48%, the hospital mortality rate decreased to zero, and the five year survival rate increased 20%.

1430 Tulane Ave. (12) (Dr. Ochsner).

DISTRIBUTION AND EXCRETION OF RADIOACTIVE ISONIAZID IN TUBERCULOUS PATIENTS

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Isoniazid (isonicotinic acid hydrazide) is a potent tuberculostatic agent, which has been widely used clinically since its introduction less than a year ago.[1] Final evaluation of its clinical effectiveness cannot be made for several years, but present evidence suggests that it will find a permanent place in the chemotherapy of tuberculosis. To obtain a better understanding of the distribution and excretion of this drug in the tuberculous patient, a series of studies has been undertaken with the use of isoniazid labeled with radioactive carbon (C^{14}). The isotopically labeled isoniazid was synthesized by Murray and Langham [2] and supplied to us by the Health Division of the Los Alamos Scientific Laboratory, Los Alamos, N. Mex. It is labeled with C^{14} in the carboxyl position and has an activity of 48.8 μc per milligram. The isotope tracer technique provides an extremely sensitive and relatively simple method of determining small amounts of drugs in tissue and body fluids. A previous paper describes the distribution of C^{14}-labeled isoniazid in normal mice.[3] This report is a study of four experiments in three patients and presents the distribution of isoniazid in normal and tuberculous tissues in man.

METHODS AND MATERIALS

Dosage.—The choice of an acceptable dose of C^{14}-labeled isoniazid was based on the experience of other workers who have used radiocarbon in human subjects. It was desirable to use an amount that would permit the accurate measurement in blood, urine, and tissues when as little as 1% of the dose remained in the body. It was also desirable to use a sufficiently small dose so that it could be repeated on two or three occasions. The University of Chicago Clinics Radioisotope Committee approved repeated doses of 400 μc (approximately 6 μc per kilogram of body weight); but experience demonstrated that as little as 3 μc per kilogram (or a total of approximately 200 μc) was adequate from the standpoint of instrumentation. Estimates of the integrated dose of radiation the subjects might receive were based on the experience of Berlin and his co-workers with glycine–C^{14}.[4] They calculated that even if there were no elimination of the C^{14} 100 μc can still be considered a safe tracer dose, since it will deliver on the average less than 0.006 r per day of radiation to the tissues. In mice the excretion of isoniazid is more rapid than that of the radiocarbon from glycine–C^{14}. In the "Summary of the Conference on the Toxicity of Carbon^{14}," Brues and Buchanan [5] estimated that the dose of nicotinic acid for man, to give the accepted tolerance exposure of 0.3 rep per week, was approximately 14.7 mc. On the basis of these two estimates, and employing a factor of safety of approximately 10, it seemed entirely proper to administer doses of 0.2 to 0.4 mc. on two or three occasions to human subjects.

A sodium chloride solution of labeled isoniazid was prepared to contain 2 mg. per milliliter. This solution had an activity of 3.6×10^6 disintegrations per second (dps) per milliliter as measured by internal gas flow counters. Prior to administration 100 mg. of unlabeled drug was added to the dose of labeled compound. This radioactive solution was injected intramuscularly. Before withdrawing the needle the syringe was detached, refilled with several milliliters of sodium chloride, and the sodium chloride wash was injected into the same site.

These experiments were conducted on three patients. The first patient had active pulmonary tuberculosis, the second had tuberculous adenitis, and the third had a tuberculous pleural effusion. The first patient received two tracer doses of labeled isoniazid 25 days apart, and the other two patients received one dose each.

From the Department of Medicine (Drs. Barclay, Ebert, and Le Roy) and the Department of Pharmacology (Drs. Manthei and Roth), University of Chicago.

The carbon-14 (C^{14}) used for the synthesis of this compound was obtained on allocation from the Isotope Division, U. S. Atomic Energy Commission.

This work was done under a contract between the Atomic Energy Commission and the University of Chicago. It was also aided in part by a grant from Motorola Inc. and from the Dr. Wallace C. and Clara A. Abbott Memorial Research Fund of the University of Chicago and the U. S. Public Health Service.

1. (*a*) Robitzek, E. H.; Selikoff, I. J., and Ornstein, G. G.: Chemotherapy of Human Tuberculosis with Hydrazine Derivatives of Isonicotinic Acid, Quart. Bull., Sea View Hosp. **13**: 27, 1952. (*b*) Elmendorf, D. F., Jr.; Cawthorn, W. U.; Muschenheim, C., and McDermott, W.: The Absorption, Distribution, Excretion, and Short-Term Toxicity of Isonicotinic Acid Hydrazide (Nydrazid) in Man, Am. Rev. Tuberc. **65**: 429, 1952.

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REPORT OF CASES

CASE 1.—A 40-year-old schoolteacher was found to have active pulmonary tuberculosis on routine x-ray examination in August, 1948. During the first two years of his illness he was treated sporadically with streptomycin and *p*-aminosalicylic acid, bed rest, and pneumoperitoneum, but at no time did he have an extended period of sanitarium care. He was first seen at the University of Chicago Clinics in the summer of 1950. At this time he was found to have several fairly well-defined densities in the right apex and subapex, which changed little during the subsequent two years. When he was first seen gastric washings were negative on culture and on guinea pig inoculation, but became intermittently positive after discontinuing the pneumoperitoneum in December, 1951. He was admitted to the hospital on Nov. 2, 1952, for resection of residual caseous lesions. Physical examination was essentially negative at this time except for slight dullness over the right upper field posteriorly. Routine laboratory work was essentially negative. The patient weighed 70.6 kg. and on Nov. 13 was given the first tracer dose of labeled isoniazid. He received 108.7 mg. of labeled isoniazid with a total specific activity of 430 μc. Following the first tracer dose he was started on *p*-aminosalicylic acid 10 gm. daily and isoniazid 200 mg. daily. On Dec. 8 he received the second tracer dose of 430 μc three and one-half hours before a wedge resection of the right upper lobe was performed. His postoperative course was uneventful, and he is being continued on bed rest and chemotherapy.

CASE 2.—A 23-year-old married nurse noted painful swelling of the right cervical nodes following a sore throat in July, 1952. The swelling persisted, and the patient complained of weakness and loss of appetite. She was first seen in the outpatient clinic in August, 1952, and examination was negative at this time except for enlarged, slightly tender cervical nodes on the right. A roentgenogram of the chest was negative. Laboratory studies were negative except for a positive tuberculin test at 1:1000 (OT). On Sept. 25 a biopsy was performed and the nodes were found to be tuberculous. On Oct. 12 the patient was started on 1 gm. of streptomycin every second day and isoniazid 200 mg. daily. On Nov. 20 the patient was given a tracer dose of labeled isoniazid five and one-half hours before resection of the tuberculous nodes in the right cervical region. She weighed 47.5 kg. and was given 104.5 mg. of labeled isoniazid with a total specific activity of 290.8 μc. Her postoperative course has been uneventful, the neck is now well-healed, and she is symptom-free.

CASE 3.—A 28-year-old woman was admitted to the hospital on Nov. 17, 1952. Three to four weeks prior to admission chills, fever, night sweats, and malaise developed. These symptoms were followed a week later by right chest pain, pleuritic in nature. Physical examination and chest roentgenograms revealed a right pleural effusion extending to the eighth rib posteriorly. A tuberculin test was positive at 1:10,000 and the erythrocyte sedimentation rate was 42 mm. per hour (Wintrobe method). The pleural fluid was amber colored and clear, and was sterile on culture. On Nov. 25 the patient, who weighed 66.8 kg., was given 103.5 mg. of labeled isoniazid with a total specific activity of 203 μc. Just before administering the tracer dose of isoniazid a polyethylene tube was inserted into the right pleural cavity, so that samples of pleural fluid could be removed at frequent intervals. The tube was removed after seven and one-half hours.

ESTIMATION OF RADIOACTIVITY

Water homogenates diluted to 10 ml. were made of weighed samples of tissue surgically removed, and aliquots were plated in duplicate on copper disks.[6] Water homogenates of feces and various dilutions in water of whole blood, plasma, urine, saliva, gastric juice, spinal fluid, and pleural fluid were plated in the same manner.[6] Samples of tissue and of body fluids were counted in windowless gas flow counters.[7] Corrections for self-absorption were applied and the average of the duplicate plates taken. Because of the high activity of the labeled drug as little as 0.02 μg of drug or of metabolite per gram of tissue could be determined, and this amount of activity was still detectable in blood and urine as long as a week after injection. Samples of expired air were collected in balloons at various intervals during two experiments, and $C^{14}O_2$ content was determined by an ionization chamber and vibrating reed electrometer.[8]

Calculation of the amount of drug per gram of tissue was made as follows: The total amount of radioactive material injected was divided by the number of micrograms of both labeled and unlabeled drug administered to give the number of disintegrations per second per microgram of drug. Thus the patient in case 1 was given 16,143,100 dps of radioactive material totaling 436.3 μc, and the total amount of drug administered was 109 mg., or 109,000 μg. Thus, $\frac{16,143,100}{109,000}$, or 148.1 dps, represents 1 μg of drug or metabolite. Since the wet weight of each tissue was known and the radioactivity of each tissue was measured, the micrograms of drug per gram (wet weight) of tissue could be calculated by the simple formula $\frac{\text{radioactivity of tissue sample} \times \text{aliquot factor}}{148.1 \text{ dps}}$. In case 2 unlabeled drug was not given with the labeled drug intramuscularly since the patient had just received 100 mg. of drug by mouth. In calculating the amount of drug present in tissue it was assumed that this patient had received 100 mg. of unlabeled drug plus 6 mg. of labeled compound. Since the metabolites of isoniazid have not been fully characterized and the percentage of unchanged drug not measured in the tissues, the results are expressed in microgram equivalents of drug. A microgram equivalent is defined as the tissue radioactivity equivalent to 1 μg of isoniazid injected.[9]

TABLE 1.—*Microgram Equivalents of Isoniazid in Blood and Plasma of Patient in Case 1 After Intramuscular Injection of 430 μc of Labeled Isoniazid**

Time After Injection	Plasma Levels, μg per Cubic Centimeter	Whole Blood Level, μg per Cubic Centimeter
30 min	1.48	1.46
1 hr	2.13	2.8
2 hr. 15 min	1.66	1.66
4 hr	1.36	1.23
8 hr	0.89	0.73
24 hr	0.20	0.14
52 hr	0.09	0.04
4 days	0.00	0.03
1 week	0.00	0.02

* The patient was given 1.54 mg. of labeled isoniazid per kilogram of body weight.

RESULTS

Distribution of Isoniazid in Uninfected Body Fluids.—Peak levels in blood and plasma were reached by the end of the first hour and ranged between 2.8 and 3.5 μg

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9. A microgram equivalent per gram of tissue is expressed as μg per gram throughout this report.

per milliliter. Figure 1 and table 1 show the levels in blood and plasma in the patient in case 1 during the first experiment. It can be seen that the level falls fairly rapidly during the first eight hours but appreciable amounts of drug equivalent are still present at the end of 12 and 24 hours. Levels of .40 to .60 μg per milliliter at 12 hours and .12 to .14 μg per milliliter at 24 hours were found. At the end of three days a level of .05 μg per milliliter was present in the blood of the patient in case 3, and after one week 0.02 μg per milliliter was found in the blood of the patient in case 1. If one assumes that only 50% of a microgram equivalent present in the blood is isoniazid, there is still an effective amount of drug present at the end of 24 hours, since .05 μg inhibits the growth of the tubercle bacilli. The levels in whole blood and plasma are parallel and approximately the same (fig. 1). Thus the drug diffuses freely through the red blood cell membrane but is not bound to the cell, since four sodium chloride washes remove all but a trace of activity from packed red blood cells taken at a time of peak activity in blood (one hour).

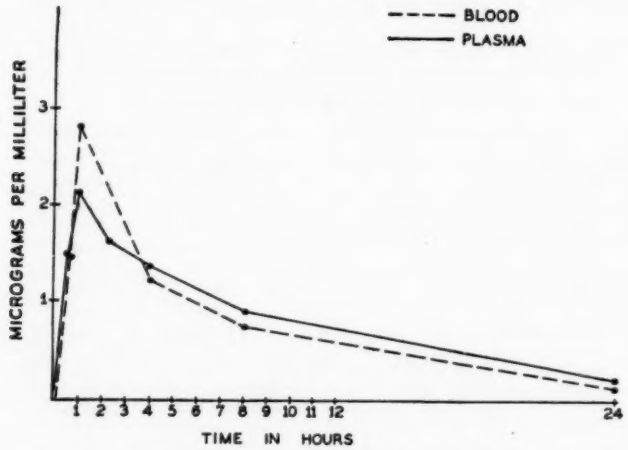

Fig. 1.—Blood and plasma levels after isoniazid administration in case 1.

One sample of spinal fluid was taken in the patient in case 1 two hours after injection. The level in the spinal fluid was 0.31 μg per milliliter at a time when the blood level was 1.66 μg per milliliter. Apparently the drug can cross the blood brain barrier in appreciable amounts even when the meninges are normal. High concentrations of activity were found in saliva in three experiments. The levels were somewhat variable, but peak concentrations were found from 0 to 3 hours after injection and varied between 1.0 and 2.52 μg per milliliter. Levels fell more gradually than in blood during the first 8 hours, but little or no activity remained after 24 hours. The concentration of drug in gastric juice was determined in only one experiment. Concentrations of 13.9 μg per milliliter at three hours and 14.9 μg per milliliter at four hours were found. Experiments are now in progress in dogs to determine if the drug is actually secreted in gastric juice.

Excretion of Isoniazid.—Drug and metabolites are largely excreted in the urine. Table 2 shows the cumulative percentage of the injected dose recovered from the urine of the patient in case 1 during the first experiment. Twenty-six per cent of the injected dose was excreted at the end of 6 hours and 84% at the end of 24 hours. A total of 92.48% of the radioactivity injected was recovered from the urine in this patient. In two other experiments 75-76% of the injected dose was recovered in the urine at the end of 24 hours. The level of radioactivity in feces was determined in two patients. In the first, 0.69% of the injected dose was excreted in three days. In the second patient, 0.61% of the injected dose was excreted in three days. In this patient 0.32% of the injected dose was excreted the first day, 0.19% the second day, and 0.12% the third day. In case 1 samples of expired air were taken at 1, 3, 6, and 24 hours. The average activity of expired carbon dioxide during this period was 0.8 dps per 100 ml. of carbon dioxide. If one assumes that a 70 kg. man at rest puts out about 200 ml. of carbon dioxide per minute, then the total expired radioactivity in 24 hours would be 2,304 dps, or 0.014% of the injected dose. Two of us (L. J. R. and R. W. M.)[3] measured the amount of $C^{14}O_2$ exhaled by mice given labeled isoniazid and found it to represent 0.017% of the injected dose. This compares with the figure 0.014% calculated for man.

TABLE 2.—*Excretion of Isoniazid in the Urine of Patient in Case 1 After Intramuscular Injection of 430 μc of Labeled Isoniazid*

Time	Cumulative Percentage of Injected Dose	Time, Days	Cumulative Percentage of Injected Dose
0-45 min.	0.02	2-4	91.58
45-90 min.	4.77	4-6	92.02
1½-3 hr.	15.44	6-7	92.14
3-6 hr.	26.35	7-8	92.23
6-24 hr.	84.15	8-9	92.30
24-48 hr.	89.73	9-10	92.39
		10-11	92.48

Distribution in Uninfected Tissues.—At the time of surgery it was possible to obtain normal as well as diseased tissue from patients in cases 1 and 2. Tables 3 and 4 show the microgram equivalents of drug per gram of normal and of diseased tissue in these two patients. The specimen of lung case 1 was taken from the resected portion of upper lobe at a considerable distance from the tuberculous lesion and appeared grossly normal. The highest concentrations of drug were found in lung and skin; the lowest were noted in fat and bone. These findings are similar to those noted in the mouse.[4] At

TABLE 3.—*Microgram Equivalents of Isoniazid Found in Various Tissues Surgically Removed from Patient in Case 1 Following the Second Tracer Dose of C^{14}-Labeled Drug**

Tissue	Time of Surgical Removal After Injection	Micrograms per Gram of Tissue	Comment
Lung	3 hr. 23 min.	1.79	.....
Caseous material	3 hr. 23 min.	0.64	2-3 cm. fluid caseous lesion
Caseous material	3 hr. 23 min.	1.04	1-1.5 cm. very dense caseous lesion
Capsule of tuberculous lesion	3 hr. 23 min.	1.88	From 2-3 cm. lesion
Muscle	3 hr. 43 min.	1.50	.....
Fat	3 hr. 45 min.	0.78	.....
Skin	3 hr. 48 min.	1.78	.....
Bone	3 hr. 52 min.	0.61	Rib

* The blood level at three hours and 45 minutes was 1.45 μg per cubic centimeter.

three hours and 23 minutes after injection the level in lung was 1.79 μg per gram of tissue, and at three hours and 48 minutes the level in skin was 1.78 μg per gram of tissue. These values were higher than the blood level at these times (1.34 to 1.45 μg per milliliter). At five hours and 10 minutes the skin level in case 2 was 1.55 μg per gram of tissue and the fat level 0.75 at a time when the blood level was 0.7 μg per milliliter. The level in various tissues as compared to the level in blood is shown graphically in figure 2.

Distribution in Tuberculous Tissue.—The portion of upper lobe removed in case 1 three hours and 23 minutes after injection of the radioactive isoniazid was cut longitudinally before fixation. Several caseous areas measuring 1 to 2 cm. in diameter were transected. One of these contained hard inspissated caseous material, and this was scooped out and used for analysis of drug content. More fluid caseous material was taken from an adjacent area. A portion of the dense fibrous capsule surrounding the dense caseous area was then removed, and all surrounding lung was cut away. This was also homogenized and an aliquot counted. It will be seen in table 3 that the dense caseous material contained 1.04 μg per gram of tissue and the more fluid caseous material had 0.64 μg per gram of wet material. The very dense capsule had the highest value of any tissue taken and contained 1.88 μg per gram of tissue.

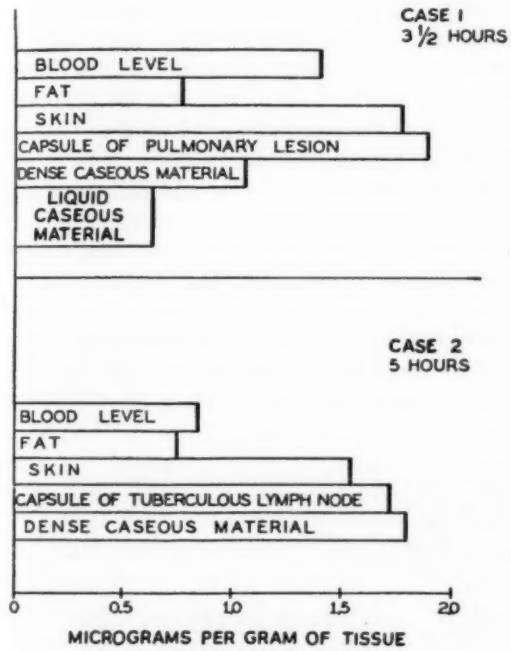

Fig. 2.—Isoniazid distribution in tissues.

The caseous nodes removed from patient in case 2 five hours and 10 minutes after injection of labeled drug were treated in a similar manner. A node with a dense capsule was cut, and separate analyses were made of the caseous material and the capsule of the node. As can be seen in table 4 the dense necrotic center of the lymph node contained the highest amount of drug equivalent present in any tissues removed at five hours (1.80 μg per gram of tissue) and the next highest concentration (1.73 μg per gram) was present in the thick capsule of the tuberculous node. Skin and muscle contained 1.55 μg and 1.50 μg per gram at the same time, and the blood level was 0.7 μg per milliliter.

Distribution in Pleural Fluid.—Table 5 shows microgram equivalents of drug found in the pleural fluid of patient in case 3. High concentrations were found after two and one-half hours, and the level remained high until seven and one-half hours, when the polyethylene tubing was removed from the pleural space. Even at the end of three days 0.06 μg per cubic centimeter of drug equivalent remained.

TABLE 4.—*Microgram Equivalents of Isoniazid Found in Surgically Removed Tissues from Patient in Case 2**

Tissue	Micrograms per Gram of Tissue
Capsule of tuberculous node	1.73
Dense caseous material	1.80
Muscle	1.50
Muscle fascia	1.44
Skin	1.55
Subcutaneous tissue	1.14
Fat	0.75

* Tissues were removed five hours and 10 minutes after intramuscular injection of 290.8 μc of radioactive isoniazid (2.2 mg. per kilogram of body weight). The blood level at this time was 0.86 μg per cubic centimeter.

COMMENT

Isotopically labeled isoniazid is rapidly absorbed into the blood stream after intramuscular injection. Peak blood levels are found in the first hour, and the rapid fall in blood level during the first eight hours is similar to that described by Rubin and co-workers [10] and Elmendorf and co-workers [1b] using chemical methods of determination. Using the more sensitive isotope tracer technique it is possible to demonstrate measurable amounts of drug in blood and plasma three to seven days after a single intramuscular injection of isoniazid. Isoniazid is freely diffusable and is found in all tissues and body fluids after intramuscular injection. Appreciable levels were found in all tissue studied at the end of three and one-half and five hours, and the data indicate that some tissue levels fall more slowly than blood levels. The highest concentrations found in normal tissues in man were in lung and skin; results similar to those found in the mouse.[4] The high concentration found in lung is of significance since

TABLE 5.—*Microgram Equivalents of Isoniazid in Pleural Fluid and Blood of Patient in Case 3 After Intramuscular Injection of 203 μc of Labeled Isoniazid**

Time After Injection of Isoniazid	Concentration in Pleural Fluid, μg per Cubic Centimeter	Blood Level, μg per Cubic Centimeter
15 min	0.15	....
30 min	0.35	....
90 min	....	2.7
2½ hr.	1.55	....
3 hr. 40 min.	1.37	....
4 hr.	....	1.63
5 hr.	1.61	....
7 hr. 20 min.	1.21	....
3 days 7 hr.	0.06	0.05

* 1.55 mg. per kilogram of body weight.

10. Rubin, S. H.; Drekter, L.; Scheiner, J., and DeRitter, E.: Determination of Blood Plasma Levels of Hydrazine Derivatives of Isonicotinic Acid, Dis. Chest **21**: 439, 1952.

pulmonary tuberculosis is the commonest form of the disease requiring chemotherapy. Two of us (L. J. R. and R. W. M.)[3] demonstrated that a drug level theoretically sufficient to produce bacteriostasis was present in mouse lung as long as a week after a single injection of isoniazid. Isoniazid is excreted chiefly by the kidneys with small amounts excreted in the feces and by the lung as carbon dioxide. Following a single dose most of the drug is excreted in 24 hours.

Tuberculosis is a disease characterized by tissue destruction and caseation. Can chemotherapeutic agents penetrate necrotic areas in sufficient concentration to influence the tubercle bacilli? This is one of the most vital and practical considerations in the therapy of tuberculosis, and no direct answer has been given to this pressing problem heretofore. The present experiments indicate that isoniazid and/or its metabolites do diffuse into dense caseous lesions and are present in high concentrations three to five hours after administration of the drug. A drug with this property is ideally suited to the therapy of tuberculosis. Work is now in progress in tuberculous guinea pigs to determine how long bacteriostatic levels of isoniazid and/or its metabolites remain in caseous areas after a single injection of drug.

The concept of combined chemotherapy in tuberculosis is now well accepted since bacterial resistance is known to develop to drugs such as isoniazid, streptomycin, or *p*-aminosalicylic acid when given alone. The present studies raise an interesting consideration as to the best drug to use in combination with isoniazid. It is possible that streptomycin does not diffuse so readily into necrotic regions and that in the absence of sufficient streptomycin in caseous areas bacterial resistance might well develop to isoniazid. It has been demonstrated by Mackaness and Smith [11] that 25 μg of streptomycin per milliliter is required to prevent further growth of intracellular tubercle bacilli, whereas isoniazid is equally active against intracellular bacilli and those grown in Dubos medium. This work indicates that isoniazid diffuses freely into the monocyte whereas streptomycin does not. It is possible that the same relationship is true in caseous areas. Radioisotope studies on the distribution of streptomycin and *p*-aminosalicylic acid in caseous lesions are contemplated.

SUMMARY

The isotope tracer technique provides an extremely sensitive and relatively simple method of determining small amounts of drug and its metabolites in tissues and in body fluids. C^{14}-labeled isoniazid has been used to study the distribution and excretion of this bacteriostatic agent in tuberculous patients. Peak levels of drug were reached in blood and plasma within an hour after intramuscular injection. Levels fell rapidly during the first eight hours, but measurable quantities of drug were found in blood and plasma three to seven days after a single injection. Isoniazid is freely diffusable and is found in appreciable amounts in uninfected tissues and body fluids, including uninfected spinal fluid of patients with tuberculosis. The highest concentrations were found in lung and skin. Isoniazid is excreted chiefly by the kidneys with small amounts excreted in the feces and by the lungs as carbon dioxide. Isoniazid diffuses freely into dense caseous lesions in both lung and lymph nodes and is present in high concentration three to five hours after injection. Isoniazid is found in pleural fluid in high concentration two and one-half hours after injection, and measurable quantities remain three days later.

6743 Cornell Ave. (Dr. Barclay).

11. Mackaness, G. B., and Smith, N.: The Action of Isoniazid (Isonicotinic Acid Hydrazide) on Intracellular Tubercle Bacilli, Am. Rev. Tuberc. **66**: 125, 1952.

ADRENALECTOMY AND OOPHORECTOMY IN TREATMENT OF ADVANCED CARCINOMA OF THE BREAST

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Thomas L-Y. Dao, M.D., Chicago

Certain cancers retain sufficient qualities of the cells from which they arose that they function in many respects like the original normal cells. When the tissue of origin is functionally dependent on hormones this property can be possessed by its neoplasms; in this case the growth of cancer is stimulated or inhibited, respectively, by the administration or the withdrawal of appropriate endocrine substances. These are the hormone-dependent tumors; among neoplasms of this sort are cancers of the breast of men and women. It is known that mammary cancer sometimes undergoes regression after excision of the ovaries, and one of us (C. H.) and a co-worker have demonstrated [1] that there is an adrenal component that sustains certain cancers of the breast since the tumors recede after adrenalectomy with maintenance of the host on cortisone. West and co-workers [2] confirmed the observation of objective improvement in mammary cancer after adrenalectomy, although in their series the clinical improvement was of only short duration.

Beatson [3] discovered that the ovary was a sustaining factor in mammary cancer in 1896, when, postulating

From the Ben May Laboratory for Cancer Research of the University of Chicago.

Cortisone acetate was provided by the Medical Division of Merck & Co., Inc., Rahway, N. J.

Dr. Eleanor M. Humphreys of the Department of Pathology of the University of Chicago assisted in the pathological interpretations.

This study was aided by grants from the Jane Coffin Childs Memorial Fund for Medical Research, the American Cancer Society on recommendation of the Committee on Growth of the National Research Council, and the Damon Runyon Memorial Fund for Cancer Research.

1. Huggins, C., and Bergenstal, D. M.: Inhibition of Human Mammary and Prostatic Cancers by Adrenalectomy, Cancer Res. **12**: 134 (Feb.) 1952.

2. West, C. D., and others: The Effect of Bilateral Adrenalectomy upon Neoplastic Diseases in Man, Cancer **5**: 1009 (Sept.) 1952.

3. Beatson, G. T.: On the Treatment of Inoperable Cancer of the Mamma: Suggestions for a New Method of Treatment, with Illustrative Cases, Lancet **2**: 104, 162 (July 11) 1896.

that the disease was due to "ovarian irritation," he observed regression in two cases of cancer of the breast after oophorectomy. Of 99 patients so treated that Lett [4] collected there was a very marked improvement in 23.2% of the patients and a distinct though less marked benefit in 13 other women. Oophorectomy soon fell in disfavor and by 1905 was seldom practiced. Since then only a few reports of oophorectomy for mammary cancer have been published, and these comprise only small numbers of cases. In part, the decline of oophorectomy as a therapeutic agent was caused by the contemporaneous development of ovarian irradiation despite the fact that this is a slower and less certain method of eliminating ovarian hormones than the surgical method.

It is known that after removal of the gonads compensatory hypertrophy and increased function of the adrenal cortex can occur. In certain stocks of mice gonadectomy induces adrenal hypertrophy with, later, the formation of adrenal cortical neoplasms and frequently the development of cancer of the breast. Also in the human male, orchiectomy is usually followed by an increase of 17-ketosteroids in the urine [5]; bilateral adrenalectomy eliminates these high values, and only trace amounts of 17-ketosteroids [6] are then found in the urine. Women who have undergone oophorectomy often continue to excrete significant and even large amounts of estrogenic compounds in the urine; these compounds disappear from the urine after adrenalectomy, as will be described.

It is clear that hormones formed in the ovary can sustain mammary cancer and that similar substances are formed in the adrenal glands in considerable amount. We now propose that these dual sources be eliminated by combined adrenalectomy and oophorectomy in cases that we shall define. A regimen [7] was devised whereby adrenal insufficiency can be regularly prevented after surgical removal of the adrenal glands [6] by substitution with cortisone and desoxycorticosterone (doca®). Patients so treated present a metabolic picture of good health [1] and are not incapacitated, although the certainty is ever present that an Addisonian crisis will ensue when the replacement is inadequate through a deficient supply of, or an excessive demand for, adrenal cortical hormones. From a practical standpoint substitution therapy is not unreasonably difficult and patients have been easily maintained in good health for at least 24 months, this state still continuing in some patients under observation. From observation of patients with mammary cancer so treated it has been learned that certain of these neoplasms commonly undergo profound and prolonged regression after adrenalectomy. An inevitably fatal neoplastic disease is treated by the induction of an easily manageable deficiency of adrenal glands; control of a cancer replaces lack of control.

CLINICAL INVESTIGATION

All of the patients had very advanced mammary cancer, and every one had distant metastases. The cases were unselected except for all having extensive disease; they were consecutive. All, save one woman, had been subjected to unilateral or bilateral mastectomy previously, usually with axillary dissection. Each case was verified by us by microscopic examination of excised tissue.

During 21 months of 1951 to 1952, 55 patients with mammary cancer were treated by adrenalectomy, 2 men and 53 women. In this series there were three deaths (5.5%) within 30 days of the operation, all in women; 50 women remain for evaluation of the therapy, the elapsed time since operation being 2 to 24 months. In 25 cases adrenalectomy alone was performed, and in 25 cases it was combined with oophorectomy. In 19 cases the adrenals and ovaries were removed in two stages about two weeks apart. We have done simultaneous adrenalectomy and oophorectomy in one procedure in six cases, finding that the double procedure has not materially added to the morbidity and there have been no fatalities. We employ a midline incision in the hypogastrium for oophorectomy followed by adrenalectomy through separate incisions in each loin. The elapsed time of adrenalectomy combined with oophorectomy is about two hours. The medical management of patients

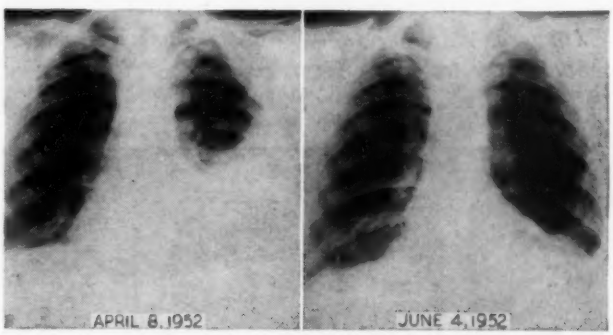


Fig. 1.—Rapid regression of pleural fluid due to metastasis of an adenocarcinoma of the breast in a man, G. S., after bilateral adrenalectomy. The fluid before operation contained carcinoma cells. Thoracentesis was not done after adrenalectomy.

who undergo adrenalectomy has been described in detail.[7] In addition we now implant three compressed pellets of desoxycorticosterone acetate (total weight, 225 mg.) subcutaneously at the time of adrenalectomy. The usual maintenance dose of cortisone acetate has been 37.5 to 50 mg. daily, and the diet is usually supplemented with 1 to 3 gm. of sodium chloride a day, both compounds being given by mouth. Regression of cancer is defined as a measurable decrease in the size or extent of the neoplasm with an improvement in general health and a gain in weight.

MAMMARY CANCER IN MEN

We treated two men with metastatic disease who had previously been subjected to orchiectomy. One patient, N. C., with pulmonary and intracranial metastases had

4. Lett, H.: An Analysis of 99 Cases of Inoperable Carcinoma of the Breast Treated by Oöphorectomy, Lancet **1**: 227 (Jan. 28) 1905.

5. Scott, W. W., and Vermeulen, C.: Studies on Prostatic Cancer: Excretion of 17-Ketosteroids, Estrogens and Gonadotropins Before and After Castration, J. Clin. Endocrinol. **2**: 450 (July) 1942.

6. Huggins, C., and Scott, W. W.: Bilateral Adrenalectomy in Prostatic Cancer: Clinical Features and Urinary Excretion of 17-Ketosteroids and Estrogen, Ann. Surg. **122**: 1031 (Dec.) 1945.

7. Huggins, C., and Bergenstal, D. M.: Surgery of the Adrenals, J. A. M. A. **147**: 101 (Sept. 8) 1951.

a considerable decrease in the size of the pulmonary metastases after adrenalectomy, but the cerebral lesions advanced and he died seven months after the operation. Another man, G. S., with extensive pleural metastases (fig. 1), had a profound regression of the lesion and

TABLE 1.—*Incidence of Metastases in Mammary Cancer of 25 Women and of Regression After Adrenalectomy*

Site of Metastasis	Incidence	Regression
Bone	20	10
Lung and pleura	7	3
Chest wall	5	2
Area producing edema of arm	6	1
Lymph nodes	4	2
Intracranial	4	2
Liver	1	1

is in good health 11 months after removal of the adrenal glands. Hemorrhagic pleural fluid, which had been accumulating rapidly in this patient despite repeated thoracentesis before adrenalectomy, has disappeared and has not reformed since the operation. Cancer cells had been found in this pleural effusion.

MAMMARY CANCER IN WOMEN

Bilateral Adrenalectomy.—The women with mammary cancer treated by removal of the adrenals alone had, it was thought, no significant ovarian function. The

Fig. 2.—Rapid regression of osteolytic metastases of mammary cancer in the terminal phalanx of a finger, with recalcification after adrenalectomy alone in a woman, M. A.

age range was 44 to 70 years; the median age was 52. All patients 52 years or less had had roentgen sterilization or oophorectomy at an earlier date. Before adrenalectomy each of the women had been subjected to various endocrine treatments: ovarian irradiation, 14 cases; oophorectomy, 4 cases; and testosterone administration, 15 cases. The principal metastases in these women and the effect of adrenalectomy thereon are summarized in table 1. To date, 9 patients have died of cancer one and

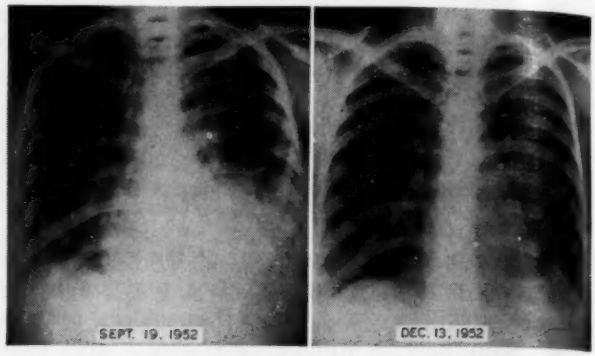


Fig. 3.—Recession of pleural and pulmonary metastases of mammary cancer after oophorectomy and adrenalectomy in a woman, M. F., aged 38. The patient had progression of the neoplastic disease despite earlier and prolonged treatment with testosterone.

one-half to seven months after operation, and 3 patients have advancing disease; we are of the opinion that 10 patients have had a regression of the disease of some magnitude. The rapidity and extent of involution of mammary cancer that can occur are illustrated in figure 2. Three patients have been operated on recently, so that the therapy cannot be evaluated now. When the course of the cancer is unmitigated by adrenalectomy, however, the therapeutic failure is apparent within two to three weeks after the operation.

Combined Adrenalectomy and Oophorectomy.—The women with mammary cancer treated by removal of adrenals and gonads were thought to have active ovarian function, although only 11 patients had menstruated within three months before the operation. The age range was 29 to 59 years, the median age being 43; the three oldest patients were 50, 58, and 59 years. Before adrenalectomy 10 of these patients had had ovarian irradiation and 15 had been treated with testosterone; despite these treatments the disease was advancing in all of the patients. Seven patients had not been subjected to previous endocrine methods of therapy. There were no

TABLE 2.—*Incidence of Metastases in Mammary Cancer of Twenty-Five Women and of Regression After Combined Adrenalectomy and Oophorectomy*

Site of Metastasis	Incidence	Regression
Bone	12	8
Lung and pleura	13	5
Chest wall	6	1
Area producing edema of arm	6	3
Lymph nodes	3	0
Intracranial	1	0
Liver	1	1

immediate postoperative deaths. Eight patients subsequently died of malignant disease 47 days to 16 months after operation, three patients present evidence of advancing disease, and in four patients insufficient time has elapsed to permit evaluation. Ten patients have had

a remission of the disease with objective evidence of improvement; the improvement occurred despite the previous failure of ovarian irradiation with roentgen rays and testosterone. The commonest areas (table 2) for regression to occur are in osseous and pleural metastases (fig. 3). It is noteworthy that extensive hepatic and intracranial lesions have regressed with the combined

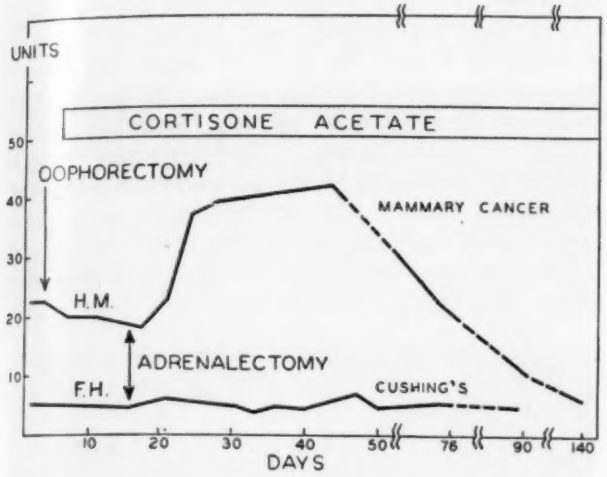


Fig. 4.—Alkaline phosphatase levels of the serum of a woman, H. M., aged 39, with mammary cancer with osseous metastases. There was no elevation of this enzyme following oophorectomy; after adrenalectomy a sharp rise occurred followed by a decline to normal values concomitant with healing osseous metastases. No rise of alkaline phosphatase occurred in the serum of a man, F. H., after adrenalectomy for Cushing's syndrome.

operation, as occurred also with adrenalectomy alone. In five cases where a remission did not ensue after adrenalectomy and oophorectomy, the patient was treated subsequently with testosterone propionate, 25 mg. per diem intramuscularly for four weeks; no benefit was observed. A similar lack of effect was observed when these women were then treated with diethylstilbestrol, 5 mg. daily by intramuscular injection.

Duration of Improvement.—Fourteen patients have been observed from one to two years after either adrenalectomy or combined excision of ovaries and adrenal glands; six of these patients are dead and one patient is living but unimproved. Seven patients are still in remission; two of these had adrenalectomy alone, while five had the combined procedure. These women appear in good health and are all somewhat obese, having gained 10 to 20 kg. in weight. The improvement also consisted of a decrease or disappearance of pain, stabilization or healing of osseous lesions, disappearance of pleural effusion, and regression and healing of recurrent lesions in postmastectomy scars. All of these patients have hot flushes, of postmenopausal kind; we regard this phenomenon as a useful prognostic sign of a favorable nature.

Serum Proteins in Mammary Cancer.—1. Preoperative: The total protein content of serum in 49 cases was in the range 6.1–7.3 gm. per 100 cc.; the mean value with standard deviation was 6.7 ± 0.6 gm. The lowest coagulable percentage of serum in 16 cases was 20% or less, values in the range for normal women; in 33 cases the value was abnormally high, 21–38%. 2. Postoperative: Data on the blood proteins are available for 16 patients who had a significant remission after adrenalectomy—alone or combined with oophorectomy. In these women the average preoperative total protein content of serum was 6.6 gm. per 100 cc.; postoperatively the average value was 7.23 gm. The average preoperative least coagulable percentage of serum was 23%; postoperatively this value decreased to 18% on average.

Alkaline Phosphatase in Serum in Mammary Cancer.—This determination is useful in studying the course of advanced mammary cancer; elevations are regarded as indicating abnormally brisk osteoblastic activity or disease of the liver. The preoperative values of women in this series are shown in table 3; in this laboratory 10 King-

TABLE 3.—*Alkaline Phosphatase in Cases of Mammary Cancer Before Adrenalectomy*

Range *	No. of Cases	Range *	No. of Cases
3.6-10	32	20.1-30	5
10.1-20	11	30.1-40	1

* Expressed in King-Armstrong units per 100 cc. of serum.

Armstrong [8] units in 100 cc. of serum is regarded as the upper limit for normal adults. Of 17 women with increased values, 2 patients had icteric serum; the high values were attributed to involvement of the liver. In 19

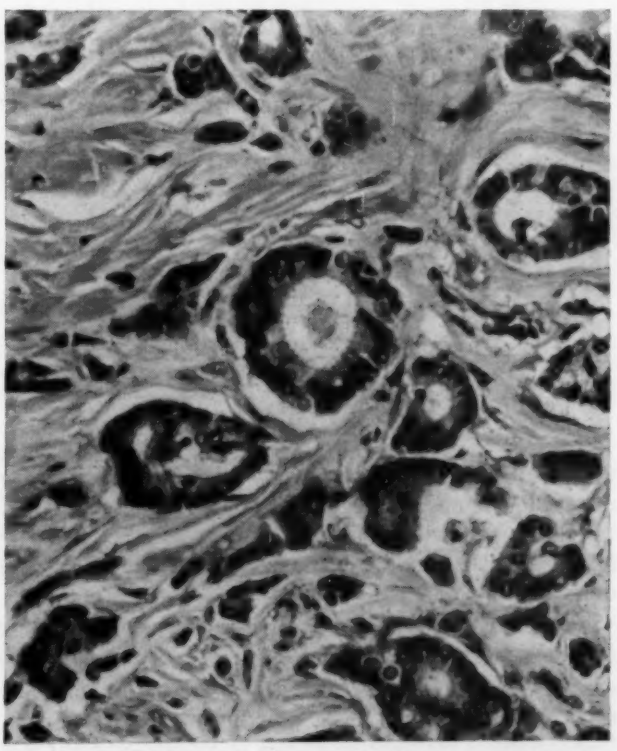


Fig. 5.—Adenocarcinoma of the breast of woman, M. R. Oophorectomy failed to induce a remission of the disease, but subsequent adrenalectomy effected a considerable regression.

cases values for alkaline phosphatase, which before operation were in the normal range, subsequently became significantly elevated; in 2 of these cases the rise

8. King, E. J., and Armstrong, A. R.: Convenient Method for Determining Serum and Bile Phosphatase Activity, Canad. M. A. J. 31:376 (Oct.) 1934.

followed oophorectomy and in 17 it occurred after adrenalectomy. In 12 cases where preoperative values ranged from 12 to 40 units, the alkaline phosphatase rose after adrenalectomy to higher levels; in 6 of these cases there was a subsequent decline to normal values after several months (fig. 4). The rise of alkaline phosphatase, with subsequent decline, concomitant with healing of osseous metastases is similar to that occurring in prostatic cancer after orchiectomy.[9]

Urinary Excretion of Estrogen in Mammary Cancer.—The content of estrogen in the urine was determined after acid hydrolysis using the weight of the uterus of the mouse as an indicator.[10] The mean values of excretion of normal women obtained in this laboratory for eight premenopausal women and four postmenopausal women, respectively, were 33 and 4.7 I. U. The preoperative values in 18 women with mammary cancer are given in table 4; 2 patients after earlier oophorectomy or ovarian irradiation had values higher than the mean that we observed for normal premenstrual women. In 12 women with mammary cancer estrogen was no longer detected in the urine after adrenalectomy and oophorectomy.

TABLE 4.—*Preoperative Urinary Excretion of Estrogen in Mammary Cancer*

Patient	Age	Ovarian Status	Urinary Excretion, I.U.* per Day
A. W.	39	Pregnancy	63.0
M. A.†	52	Roentgen castration	58.9
M. F.‡	39	Menstruating	53.8
J. D.	29	Menstruating	45.0
M. W.†	45	Surgical castration	38.1
V. B.	35	Menstruating	36.3
H. McP.‡	39	Menstruating	35.4
G. S.	50	Roentgen castration	32.5
G. A.	47	Roentgen castration	20.1
E. Z.‡	31	Roentgen castration	19.6
Z. S.†	45	Roentgen castration	16.4
C. K.†	58	Postmenopausal	16.0
S. Z.	42	Roentgen castration	15.2
A. M.†	52	Postmenopausal	14.7
M. S.	50	Roentgen castration	13.4
V. C.	47	Roentgen castration	12.3
B. V.‡	43	Menstruating	10.5
L. P.	45	Roentgen castration	4.7

* An international unit (I.U.) is 0.1 μg of estrone.
† Improved after adrenalectomy.
‡ Improved after combined adrenalectomy-oophorectomy.

Pathology.—In 47 cases the range of weight for single adrenal glands was 3.1–5.3 gm.; the average weight with standard deviation was 4.2 ± 1.1 gm. The total adrenal weight (both glands) was 6.5–10.5 gm. The weight of the adrenal glands in mammary cancer in most cases did not differ from that of normal healthy adults who have suffered accidental death. A discrete accessory adrenal gland was found in one case near the renal pedicle. Metastases of carcinoma were detected in the adrenal glands in 14 patients in this group. The medulla appeared to be the site of localization.

Dr. E. M. Humphreys evaluated the ovaries of 24 women, who had been subjected to oophorectomy, independently of the clinical findings. Primordial follicles, granulosa, and lutein cells were present in the ovaries of 11 women, all of whom had been menstruating within the three months preceding oophorectomy; two of these women had cystic ovaries. In two postmenopausal women, in each of whom the ovaries weighed more than 4 gm., there was a possibility of active ovarian function and there were hyperplastic masses of blue (hematoxylin stain) lipid-containing tissue in the ovarian stroma. In 11 women who were in the postmenopausal state or who were younger women previously treated by roentgen irradiation, the ovaries were small and sclerotic. In five cases metastases of mammary cancer were found in the ovaries.

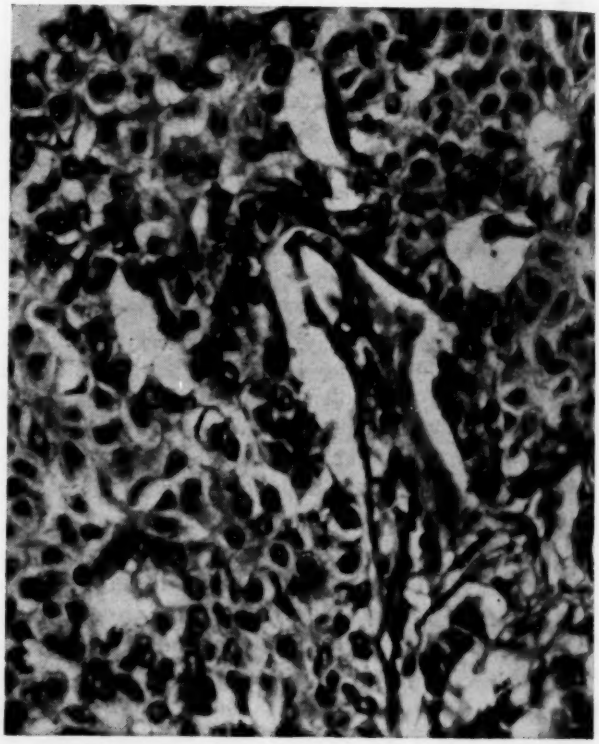


Fig. 6.—Papillary carcinoma of breast of woman, H. M.; regression of extensive metastases followed adrenalectomy and oophorectomy.

The microscopic appearance of the original neoplasm was of value in determining prognosis. The important consideration in determining response to adrenalectomy was maturity of cells with the formation of acini. The formation of glands with a single layer of cells lining the cancerous tubule and with secretion in the lumen was differentiated from the duct carcinomas with many layers of lining cells with detritus in the false lumen, apparently due to central necrosis. We divided the histological material in four classes: (*a*) adenocarcinoma, defined as a preponderance of gland formation with secretion (fig. 5), 15 cases; (*b*) papillary carcinoma (fig. 6), 4 cases; (*c*) duct cell cancers (fig. 7), 8 cases; (*d*) undifferentiated carcinoma (fig. 8), 16 cases. These categories were not always clear-cut or

9. Huggins, C., and Hodges, C. V.: Studies on Prostatic Cancer: The Effect of Castration, of Estrogen and of Androgen Injection on Serum Phosphatases in Metastatic Carcinoma of the Prostate, Cancer Res. **1**: 293 (April) 1941.

10. Evans, J. S.; Varney, R. F., and Koch, F. C.: Mouse Uterine Weight Method for Assay of Estrogens, Endocrinology **28**: 747 (May) 1941.

easily separable, and there were intergrades between them. Moreover we realize that it is an oversimplification to deduce function of cells with precision from morphological characteristics in all cases. Despite these difficulties we are of the opinion that it was usually possible to correlate histological appearance in a useful manner with response to the operations employed. Only one patient with a duct cell cancer responded favorably to steroid withdrawal; no case of undifferentiated car-

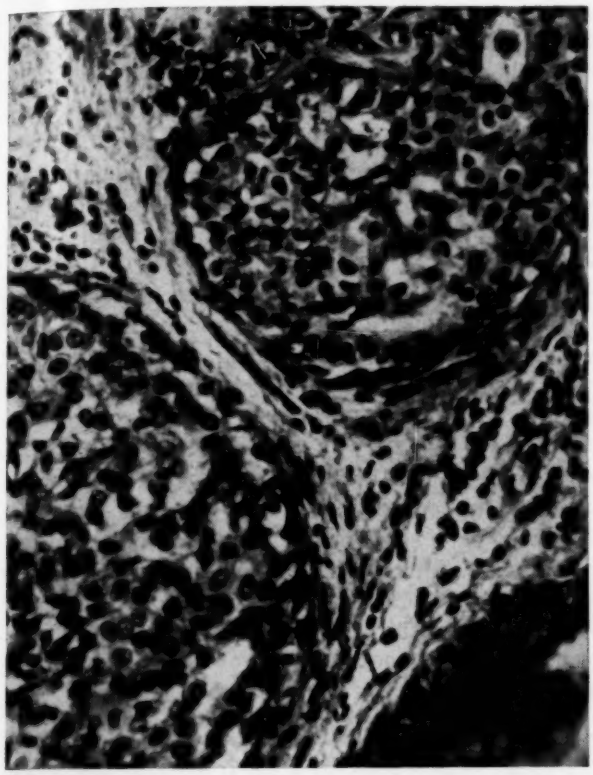


Fig. 7.—Mammary duct carcinoma of a woman, R. C. No improvement occurred following adrenalectomy.

cinoma improved. Of 19 patients with adenocarcinoma and papillary carcinoma, 16 had a remission of the malignant process after adrenalectomy alone or after this operation combined with oophorectomy. In this series there were six cases where the interval between mastectomy and adrenalectomy was very prolonged, the interval being 6½ to 16 years; all of these patients responded favorably and all had adenocarcinoma. Those mammary cancers with pronounced acinus formation evidently grew at a slower rate than undifferentiated or duct carcinomas.

COMMENT

It is certain that the ovary is strongly implicated in the maintenance of mammary cancer in the human female, although the relative function of each of the ovarian hormones in this regard is not well understood. Lacassagne discovered that estrogen is an important factor in the pathogenesis of neoplasms of the breast in the mouse, but the widespread, and at times indiscriminate, use of estrogens in clinical medicine has not appreciably increased the incidence of breast cancer. Estrogen alone does not furnish optimal development of the breast in humans where ovarian function is deficient.

The involution of mammary cancer after oophorectomy is clearly due to removal of hormones formed in the ovary; the most reasonable explanation of the beneficial effects of adrenalectomy is the elimination of hormones of a similar type. The excretion of estrogen in the urine of women who have undergone oophorectomy is abolished by adrenalectomy. Since there is a dual supply of hormones of ovarian type, both sources should be eliminated in cancer of the breast when they contribute importantly to the endocrine pool. The development of hot flushes of the kind that occur in postmenopausal women was a favorable prognostic sign after steroid withdrawal in mammary cancer; this phenomenon seems to be related to an increased function of the pituitary since it is associated with high titers of gonadotrophin in the urine. This type of increased pituitary activity clearly is not inimical to regression of mammary cancer.

Regression of mammary cancer after deprivation of steroids by surgical means is a function of removal of critical amounts of sustaining hormones together with sufficient maturity of the neoplastic cells that they are dependent on hormones—it depends on hormone production plus reactivity of cells. Mammary adenocar-

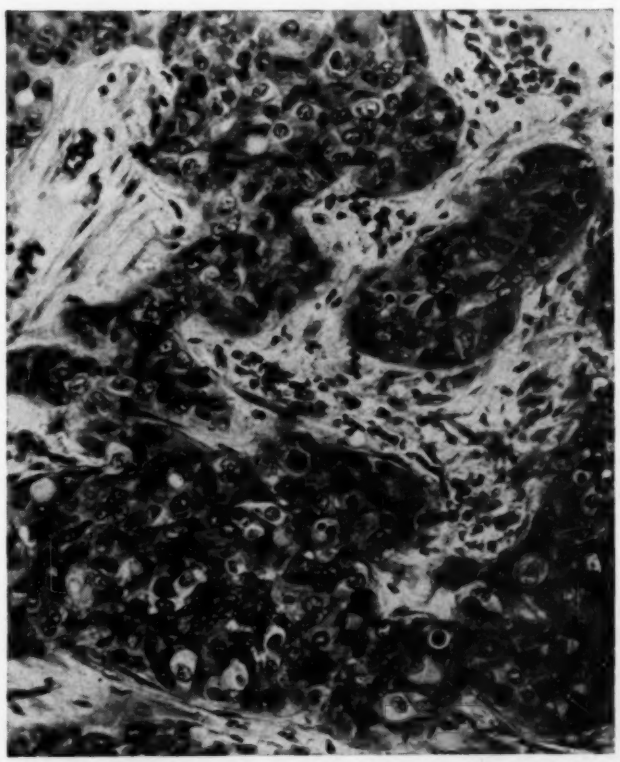


Fig. 8.—Undifferentiated carcinoma of breast of woman, R. B. No improvement resulted from adrenalectomy.

cinoma usually fulfills the latter requirement and so constitutes a special category of breast cancer contrasted to ductal and undifferentiated carcinoma. Halberstaedter and Hochman [11] observed earlier that adenocarci-

11. Halberstaedter, L., and Hochman, A.: The Artificial Menopause and Cancer of the Breast, J. A. M. A. 131: 810 (July 6) 1946.

noma of the breast responded to ovarian irradiation more commonly than carcinoma simplex.

We consider that the formation of the acini in mammary carcinoma is a positive process directly attributable to secretion induced by hormones. In our theory the lumen of the acinus cannot be empty—it contains secretion; otherwise it would be filled by the ingrowth of cells as is the lumen of the tubule in ductal carcinoma. Many of the cancers derived from the lobule-alveolar apparatus of the breast are hormone-dependent in contrast to those arising from ducts. The elimination of critical amounts of supporting hormones from the internal environment of certain cancers alters cell metabolism sufficiently to stop secretion causing the acini to collapse and the cells to shrink [1] with subsequent benefit to the patient.

With any treatment in medicine, particularly one of some complexity, the question must be decided whether it is worth while for the patient. Simple methods are available that at times restrain advanced mammary cancer. These are roentgen irradiation of the ovaries and the administration of androgenic and estrogenic substances; the treatment with sex hormones is empirical in origin. The mean survival times of patients treated in large series is as follows: with palliative irradiation, 12 months; with testosterone propionate, 7.5 months [12]; and with estrogens, 7.6 to 12.3 months.[12] The evidence that we have presented in the present small series indicates that the survival after adrenalectomy and oophorectomy is longer. Further these surgical procedures have induced important remission in patients in whom irradiation and testosterone were ineffective. In this group of mammary adenocarcinomas the surgical methods have provided relief not otherwise possible at present.

We are of the opinion that in certain cases in the present series the ovaries of postmenopausal women had active endocrine function that made oophorectomy desirable in this group. Oophorectomy remains a simple, certain, and abrupt method of eliminating ovarian hormone production and for these reasons seems to be more desirable than irradiation of the pelvis in the treatment of mammary cancer.

SUMMARY

When the gonads and adrenal gland are removed from men and women the level of physiologically active steroids is very greatly reduced in amount. Judged from different rates of growth of various mammary neoplasms in this artificial steroid-poor environment, cancer of the breast is not a single pathological state but consists of categories that differ in clinical and functional characteristics. Some of these neoplasms in both sexes are composed of cells of sufficient functional maturity that they undergo a decrease of activity when critical quantities of supporting hormones are removed through surgical removal of these sources; the patient is benefited in this circumstance. Other mammary cancers are immature and do not respond favorably to the withdrawal of steroid hormones.

The microscopic appearance of the neoplasm is frequently of value, as a first approximation, in differentiating between dependent and nonresponsive cancers. Most of the cancers that were predominantly papillary neoplasms or adenocarcinomas regressed after the surgical procedures; duct carcinomas rarely and undifferentiated mammary cancers never responded favorably. These histological criteria, while not invariably permitting a successful prediction of functional response, or its lack, were helpful. The determination of the titer of estrogenic substances in the urine preoperatively was also useful in the clinical management of cancer of the breast; high values in the absence of gonadal function indicate adrenal cortical activity of significance in mammary cancer.

Adrenalectomy or this operation combined with oophorectomy has induced significant and prolonged regression of extensive mammary cancers of women who had not responded to earlier treatment with testosterone and roentgen irradiation of the ovaries. Adrenalectomy alone has provided a remission in men and women in whom the disease was advancing despite removal of testes or ovaries. The surgical methods are useful therapeutic agents in appropriate cases of cancer of the breast in the human male and female.

The mechanism of improvement after adrenalectomy in cancer of the female breast seems to be the withdrawal of critical amounts of hormones similar to those formed in the ovary. After adrenalectomy in women who have undergone oophorectomy the excretion of estrogen in the urine is abolished. Increased pituitary activity of the type that occurs in postmenopausal women is not incompatible with regression of mammary cancer.

950 E. 59th St. (Dr. Huggins).

12. Current Status of Hormone Therapy of Advanced Mammary Cancer, report of the Council on Pharmacy and Chemistry J. A. M. A. 146: 471 (June 2) 1951.

Retraining of the Disabled.—Although we have excellent hospitals, public health centers and other facilities for preventive and definitive medicine in various parts of the world, there are, in comparison, but a small handful of facilities equipped to provide for the patient with a physical disability the necessary retraining in physical skills which are a requisite for later vocational training. In the past, the physician has thought too much about the physiologic and clinical aspects of the patient's disability. The vocational counselor too frequently has thought only in terms of physical skills which could be utilized vocationally. Between the two, however, there is a wide area through which most physically handicapped persons must go when their medical care is completed but before they are ready to undergo vocational training. In this area lies the physical retraining in skills necessary for the carrying on of the activities inherent in daily living and common to all types of work.

Except in a few isolated instances, the physically handicapped person must be retrained to walk and travel, to care for his daily needs, to use normal methods of transportation, to use ordinary toilet facilities, to apply and remove his own prosthetic devices, and to communicate either orally or in writing. These are such simple things that they are frequently overlooked, but the personal, vocational and social success of the handicapped person is dependent upon them.—H. A. Rusk, M.D., Total Rehabilitation, *Journal of the National Medical Association*, January, 1953.

"STILBAMIDINE" IN THE TREATMENT OF CUTANEOUS BLASTOMYCOSIS

REPORT OF A CASE

Major Joel C. Fink, Capt. Darl E. VanderPloeg
and
Lieut. Col. Myles P. Moursund (MC), U. S. Army

Since North American blastomycosis was first reported by Gilchrist [1] in 1896, numerous forms of treatment have been reported as useful in the management of this disease. Some measure of success in the management of cutaneous blastomycosis has been obtained in the past through the use of iodides, superficial roentgen ray therapy, local destructive measures, and hyposensitization with blastomycin vaccine. Other forms of therapy have been used with only partial success. In spite of the successive advent of the recent antibiotics and chemotherapeutic agents, the treatment of blastomycosis has remained unsatisfactory. Recently "stilbamidine" (4,4'-stilbenedicarboxamidine) has been reported to be effective in the treatment of a limited number of cases of systemic North American blastomycosis. These encouraging results suggested the use of "stilbamidine" in the treatment of primary cutaneous blastomycosis. Experience with the use of "stilbamidine" isethionate in the treatment of a patient with cutaneous blastomycosis is, therefore, described.

REPORT OF A CASE

A 41-year-old white man was admitted to the dermatology section of Brooke Army Hospital on Feb. 15, 1952, with a tentative diagnosis of North American blastomycosis. The following information was obtained from the medical records available at the time of admission. In August, 1951, routine chest roentgenograms revealed large feathery areas of increased density extending from the hilar regions into the lung bases. From August, 1951, to November, 1951, serial chest roentgenograms were obtained in the outpatient department of a military hospital in England. The findings were suggestive of pulmonary tuberculosis or coccidioidomycosis. All laboratory studies, including examinations of sputum for fungi and bacteria, were negative on repeated occasions. Intradermal tuberculin tests were negative at 24 and 48 hours. A roentgenogram of the chest on Nov. 20, 1951, showed considerable clearing of the pulmonary infiltrate, and subsequent chest roentgenograms were reported to be within normal limits. After several months of observation it was concluded that the pulmonary changes were representative of a primary atypical pneumonia.

An elevated nodule was first noted on the posterior neck in July, 1951, while the patient was stationed in England. This initial lesion was present during the outpatient visits in August and September, 1951, but was not described until late October, 1951, when two nodular lesions were noted on the posterior neck (fig. 1*A*). In November, 1951, similar lesions appeared on the face, left supraorbital area (fig. 2*A*), right hand (fig. 1*B*), upper chest, and right thigh. Hanging drop preparations of the discharge from the lesions examined at that time revealed the presence of small doubly refractile, oval and round bodies resembling blastomycetes. Repeated cultures on various laboratory media were performed at a laboratory in England but failed to reveal any pathogenic fungi. The patient was referred to a dermatologist in Liverpool who felt that the patient had primary cutaneous North American blastomycosis. This physician recommended treatment with superficial roentgen ray therapy, large doses of potassium iodide, and an ointment containing benzoic and salicylic acid. In addition to the daily oral administration of 10 gm. of potassium iodide, roentgen therapy consisting of 325 r (75 kv., no filtration) was delivered in divided doses to six areas of the face and neck during November and December, 1951. There appeared to be definite healing and involution of some of the lesions on this regimen, but the lesions on the cheeks and posterior nuchal area enlarged. No treatment other than undecylenic acid ointment locally was used during the period of Jan. 15, 1952, through Feb. 15, 1952.

On admission to this hospital the patient complained of moderately severe recurrent bilateral temporal headaches unassociated with nausea or vomiting. Physical examination was within normal limits except for the cutaneous lesions of the face and neck, moderate bilateral hearing loss, and multiple condyloma acuminata in the anal region. There were multiple well-healed, nontender scarred areas showing peripheral pigmentation and central atrophy on the left side of the neck, upper chest, right thigh, right hand, and left supraorbital area. There was a verrucous crateriform lesion with a sharply elevated margin measuring 2 cm. in diameter on the left malar eminence. The surface of this lesion was covered with many fine papillary projections and had a dusky erythematous hue. On pressure a small amount of purulent material was readily expressed from numerous small orifices on the surface of the lesion. There was a similar lesion measuring 2.5 cm. in diameter over the right malar eminence (fig. 3*A*). Two small nodular areas measuring 3 to 6 mm. in diameter were also noted in the posterior nuchal region.

Laboratory studies, including blood counts, urinalyses, roentgenograms of the chest and skeletal system, and an electrocardiogram, were all within normal limits. An electroencephalogram and a cerebrospinal fluid examination were performed as part of a thorough neurological work-up, and no abnormality was found. It was the consensus of opinion of the allergist, internist, and neurologist that the patient's headaches were on a psychogenic basis. Since hepatic and renal toxicity due to "stilbamidine" have been reported in animals,[2] liver and kidney function tests including sulfobromophthalein (bromsulphalein®), phenolsulfonphthalein, van den Bergh, and cephalin flocculation were performed before and after treatment with "stilbamidine." All results were normal. A 4 cm. zone of erythema and 1 cm. of induration occurred at the site of the injection of 0.1 cc. of a 1:100 dilution of standardized heat-killed blastomycin vaccine. An intradermal coccidioidin test (0.1 cc. of a 1:100 dilution) was negative after 48 hours.

Several direct wet preparations of the pus from the facial lesions revealed occasional thick-walled, doubly refractile cells. These cells measured approximately 10 to 15 μ in diameter and showed only single budding. These cells were considered to be typical Blastomyces dermatitidis organisms. Histopathological study of tissue obtained in February, 1952, from a lesion on the posterior neck revealed a chronic granulomatous infiltrate. Double refractile, thick-walled budding cells were seen in some of the giant cells (fig. 3*B*). No pathogenic fungi

Dr. J. Lewis Pipkin and Captain E. Randolph Trice assisted in the preparation of this article.

The "stilbamidine" isethionate used in this study was supplied by the William S. Merrell Company, Cincinnati.

From the Dermatology and Syphilology Section, Brooke Army Hospital, Fort Sam Houston, Texas (Captain VanderPloeg and Lieutenant Colonel Moursund, Chief of Section), and U. S. Army Hospital, Fort Knox, Ky. (Major Fink).

1. Gilchrist, T. C.: A Case of Blastomycetic Dermatitis in Man, Johns Hopkins Hosp. Rep. **1**: 269, 1896.

2. Schoenbach, E. B.; Miller, J. M., and Long, P. H.: The Treatment of Systemic Blastomycosis with Stilbamidine, Ann. Int. Med. **37**: 31 (July) 1952.

were grown despite repeated cultures on Sabouraud's media and on blood agar.

Superficial low voltage roentgen ray treatment consisting of 350 r in divided doses of 150 and 200 r given at 10 day intervals was administered to the lesions on the face in February, 1952. The factors employed were 90 kv., 5 ma., 17 cm. skin focal distance, and a 1 mm. Al filtration. The inherent filtration was 0.5 mm. Al, and the half-value layer of 1 mm. Al. A total of 675 r was thus delivered to the malar lesions from November, 1951, through February, 1952. Similarly a total of 300 r in 150 r doses at eight day intervals was administered

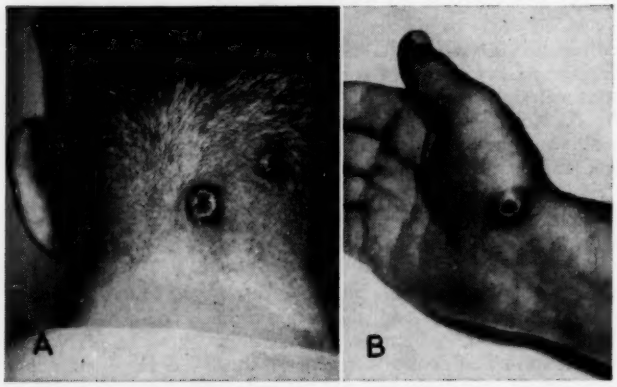


Fig. 1.—*A*, nodular and crateriform lesions of blastomycosis on neck, and *B*, crateriform lesion of blastomycosis on right hand prior to any type of treatment.

to a pair of nodular lesions on the posterior neck in March, 1952. The neck lesions persisted; therefore, following partial excision of one of the lesions for biopsy purposes, these lesions were destroyed by curettage and electrodesiccation. Because of the initial sensitivity demonstrated by the blastomycin intradermal test, the patient received intradermal and subcutaneous blastomycin in increasingly larger doses twice weekly until a total of 5 cc. of 1:100 dilution of the heat-killed vaccine had been administered. Following the initial dose of 0.1 cc., each subsequent dose was increased 0.2 cc. until 1 cc. of the vaccine was being administered two times weekly. In spite of the combined roentgen ray therapy and blastomycin desenstization, the lesions on the malar eminences showed progressive enlargement and no evidence of involution. The lesions on the posterior neck healed with minimal residual scarring.

"Stilbamidine" therapy was instituted on March 29, 1952. The treatment schedule and technique of administration of

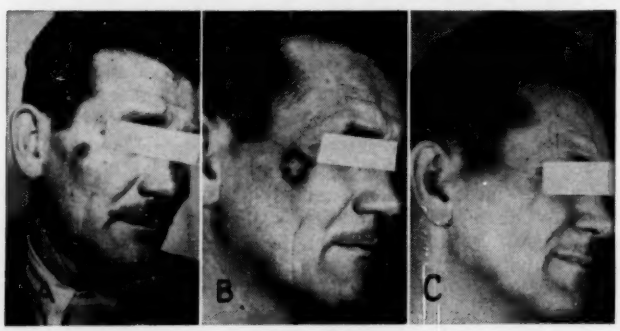


Fig. 2.—*A*, nodular lesions of blastomycosis on right malar eminence and left supraorbital area prior to any type of treatment (November, 1951); *B*, right malar lesion following first course of "stilbamidine" (50-60% involution) (April, 1952); and *C*, complete healing two months after completion of therapy (August, 1952).

"stilbamidine" was similar to the one used by Schoenbach and his co-workers.[3] "Stilbamidine" isethionate was administered by slow intravenous drip in combination with 200 cc. of 5% glucose in distilled water. An initial dosage of 0.05 gm. was given daily for three days followed by 0.1 gm. daily for three more days. On the seventh treatment day the dosage was increased to 0.15 gm., and this amount was continued daily for nine days. While receiving this treatment the patient was maintained on a low protein, low purine diet as recommended by Schoenbach and co-workers.[3] A total of 1.8 gm. of "stilbamidine" was administered during the initial treatment period. The patient remained essentially symptom free and demonstrated no ill-effects from this treatment. On completion of this first course of "stilbamidine" therapy, a biopsy was taken from the lesion on the right malar eminence. Histopathological study of the tissue specimen revealed minimal granulomatous infiltrate and no evidence of blastomycetes (fig. 4). The patient was examined again on May 6, 1952, at which time it was estimated that there had been 50 to 60% involution of the active lesions on the face (fig. 2*B*).

A second course of "stilbamidine" was instituted on May 26, 1952, 44 days after the completion of the first course of treatment. A dosage of 0.15 gm. was given daily for 13 days in the same manner as previously described. The patient received a total of 3.75 gm. of "stilbamidine" during the two courses of treatment. Rapid and complete involution of the malar lesions was noted during the second course of treatment leaving only residual scarring at the completion of treatment. Examination two months later revealed very minimal scarring in the previously involved areas of the face (fig. 2*C*). No new lesions were noted. Further examination three months after the completion of therapy revealed the same good cosmetic result and no evidence of new lesions.

One month after the completion of "stilbamidine" therapy the patient complained of mild numbness and formication over

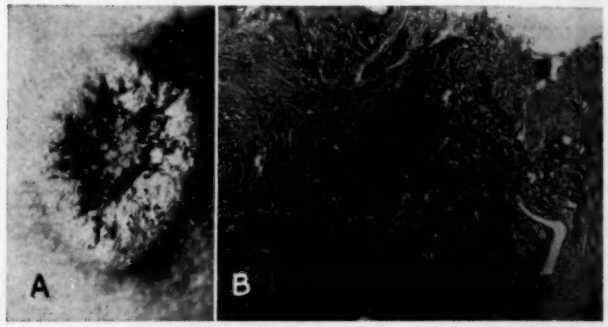


Fig. 3.—*A*, verrucous and crateriform lesion of blastomycosis on right malar eminence persisting after roentgen ray therapy, iodides, and blastomycin hyposensitization but prior to "stilbamidine" therapy, and *B*, biopsy of lesion on posterior neck prior to "stilbamidine" therapy showing granulomatous infiltrate and blastomycete in giant cell.

the forehead, nose, malar areas, and upper lip. This feeling of numbness was associated with a spotty analgesia and was interpreted by the neurologist to be a trigeminal neuropathy, which was probably a manifestation of "stilbamidine" toxicity. This neuropathy has persisted to the present time, three months after completion of "stilbamidine" therapy.

COMMENT

As an outcome of an effort to discover compounds with chemotherapeutic properties and in an effort to find drugs with trypanocidal action of low toxicity, considerable information has become available in the past 15 years relative to the biological application of the various drugs of the aromatic diamidine series. Among several hundred compounds screened against several species of trypanosomes as well as against bacteria and fungi, "stilbamidine" along with "propamidine" (4:4'diamidinodiphenoxypropane dihydrochloride), "pentamidine" (4,4'-[pentamethylenedioxy]dibenzamidine), and phenocole ("phenamine") hydrochloride were selected as most promising for clinical investigation. These drugs demon-

3. Schoenbach, E. B.; Miller, J. M.; Ginsberg, M., and Long, P. H.: Systemic Blastomycosis Treated with Stilbamidine: A Preliminary Report, J. A. M. A. **146**: 1317 (Aug. 4) 1951.

strated antifungicidal properties in addition to their antibacterial and antitrypanosomal effects.[4]

W. O. Elson [5] first reported in vitro sensitivity of blastomycetic dermatitis to "propamidine" in 1945. Colbert, Strauss, and Green [6] also demonstrated in vitro sensitivity of blastomycetic dermatitis to "propamidine" and found that complete inhibition of growth was present at a concentration of 7.5 μg of "propamidine" per cubic centimeter of agar. These investigators reported one case of cutaneous blastomycosis that clinically improved coincidently with the local application of "propamidine" incorporated in 9% cellulose gel to a concentration of 0.1%. Curtis and Harrell [7] demonstrated inhibition of blastomycetic dermatitis by a concentration of 0.01 mg. of "stilbamidine" per cubic centimeter of agar. Four

Fig. 4.—Biopsy of right malar lesion after first course of "stilbamidine" therapy, showing chronic round cell infiltration but no giant cells or blastomycetes.

patients with systemic blastomycosis were treated with "stilbamidine" by Schoenbach, Miller, and Long.[2] Beneficial results were obtained in three patients, and an encouraging result was noted in a fourth patient. Excellent clinical response has been recently reported by Curtis and Harrell [7] following the use of "stilbamidine" in two cases of systemic blastomycosis.

In regard to the toxicity of these drugs, several thousand patients, including many poor risk, chronically ill Asiatic and African natives with kala-azar, have been treated with one or more of the diamidines and no fatalities have been attributed to these drugs.[4] Immediate vascular reactions including fall in blood pressure, flush, dizziness, sweating, headache, nausea, and vomiting may occur.[4] A local thrombophlebitis is frequently seen after the administration of concentrated solutions of the diamidines intravenously.[4] Neuropathy of the fifth cranial nerve appears to be the commonest side-effect from treatment with "stilbamidine" and has been reported by many investigators.[8] The mechanism of this neuropathy is obscure [4]; the dosage of "stilbamidine," route of administration, speed of injections, and severity of immediate reaction do not appear to influence the occurrence of neuropathy.[9] This delayed toxic effect occurred in a fairly high percentage of cases two to five months after a course of "stilbamadine."[8] Paresthesia, anesthesia, hypalgesia, and numbness are the commonest symptoms, although tingling and formication also occur.[8] Often these symptoms slowly disappear after a period of several months, but in others they seem to persist indefinitely.[8] A fifth nerve neuropathy appeared in three of four patients with blastomycosis, treated with "stilbamidine" by Schoenbach, Miller, and Long [2] one to four months after the completion of treatment. Curtis and Harrell [7] reported no evidence of toxicity to "stilbamidine" in two cases of systemic blastomycosis treated with this drug.

SUMMARY

"Stilbamidine," an aromatic diamidine of the stilbene group, has been used in the treatment of a patient with cutaneous North American blastomycosis. Older forms of treatment including roentgen ray therapy, iodides, and blastomycin hyposensitization were only partially effective in clearing some of the lesions present in this case and totally ineffective in controlling other lesions. Following the first course of 1.8 gm. of "stilbamidine" an estimated 50 to 60% involution of lesions occurred. No immediate toxic reactions were noted. After a rest period of 44 days a second course of 1.95 gm. of "stilbamidine" was given. Complete involution of the lesions occurred after a total dosage of 3.75 gm. of "stilbamidine." There has been no recurrence of the lesions three months after the completion of therapy.

A mild trigeminal neuropathy consisting of numbness and formication over the forehead, nose, malar areas, and upper lip was first noted one month following the last course of treatment. This neuropathy was considered to be a toxic manifestation of the "stilbamidine" therapy. However, it is felt that trigeminal neuropathy is not a serious enough complication to be considered a contraindication to the use of "stilbamidine" in view of the excellent clinical response shown in this case of recalcitrant cutaneous blastomycosis. It is felt that "stilbamidine" is a promising agent for the treatment of cutaneous North American blastomycosis and warrants further clinical trial.

4. Schoenbach, E. B., and Greenspan, E. M.: The Pharmacology, Mode of Action and Therapeutic Potentialities of Stilbamidine, Pentamidine, Propamidine and Other Aromatic Diamidines: A Review, Medicine **27**: 327 (Sept.) 1948.

5. Elson, W. O.: The Antibacterial and Fungistatic Properties of Propamidine, J. Infect. Dis. **76**: 193 (May-June) 1945.

6. Colbert, J. W., Jr.; Strauss, M. J., and Green, R. H.: The Treatment of Cutaneous Blastomycosis with Propamidine: A Preliminary Report, J. Invest. Dermat. **14**: 71 (Feb.) 1950.

7. Curtis, A. C., and Harrell, E. R., Jr.: The Use of 2 Stilbene Derivatives (Diethylstilbestrol) and Stilbamidine in the Treatment of Blastomycosis, to be published.

8. Schoenbach and Greenspan.[4] Sen Gupta, P. C.: Cerebral Lesions in Dogs Following Injections of 4:4'-Diamidino-Stilbene, correspondence, Tr. Roy. Soc. Trop. Med. & Hyg. **40**: 508 (March) 1947. Napier, L. E.: Urethane and Stilbamidine in Multiple Myeloma, correspondence, Lancet **2**: 489 (Sept. 27) 1947. Sati, M. H.: Post-Stilbamidine Neuropathy, with Reference to the Retention of the Drug in the Body, Ann. Trop. Med. **43**: 4 (April) 1949.

9. Schoenbach and Greenspan.[4] Curtis and Harrell.[7]

SMOKER'S RESPIRATORY SYNDROME, A CLINICAL ENTITY

George L. Waldbott, M.D., Detroit

In 1950, Myerson [1] described a lesion of the vocal cords due to irritation from smoking. This, he stated, originates from a circumscribed edema that gives way to an inflammatory lesion and later assumes the appearance of an edematous fibroma. Myerson observed this condition in 143 smokers who consulted him because of vocal fatigue and hoarseness. In one case, the lesion had caused an obstruction in the larynx requiring a tracheotomy. No reference was made to changes in the pharynx and other parts of the upper respiratory tract that are exposed to irritating smoke at least as much as the larynx. One would expect to encounter similar changes in these areas.

Literature concerning the effect of smoking on the human organism deals mainly with cardiovascular changes, such as tachycardia, angina pectoris, vasoconstriction of peripheral blood vessels, and hypertension. Extensive work has been done by Harkavy [2] concerning sensitivity to tobacco and the effect of tobacco on vascular diseases. As for respiratory symptoms, there has been a great deal of speculation concerning the development of cancer of the lungs from smoking; otherwise, the literature is scant. My interest in this problem is based on the following experience.

In February, 1949, I had an unusually severe upper respiratory catarrh. This illness was preceded by similar but less severe episodes occurring frequently over a number of years. This acute phase in the upper respiratory tract gradually changed to a descending catarrh with expectoration of purulent sputum. During the following weeks, a chronic cough developed and was accompanied by asthmatic wheezing, dyspnea, and a sensation of constriction and tightness in the trachea and upper bronchial tree. This condition persisted for approximately nine months. On several occasions, the wheezing became so intense that it awakened me at night, but it was controlled by the use of antihistaminics. As a rule, when a moderate amount of mucus had been expectorated, the wheezing subsided. It returned only for short intervals during the day and followed exposure to dust, smoke, or irritating fumes. Three or four times I experienced chest pains that appeared suddenly without apparent cause, radiated into the arms and neck, and lasted from 5 to 10 minutes.

Because of the absence of a personal or family background of bronchial asthma or other clinical features of this disease, an allergic causation was ruled out. A chest x-ray, sputum examinations for fungi and eosinophil cells, an electrocardiogram, eyeground examinations, and spirometric recordings revealed nothing abnormal. On several occasions, I observed that the wheezing was precipitated by smoking, especially by inhalation of the smoke, and that coughing and wheezing were more pronounced on Monday mornings. This coincided with the fact that on Sundays I smoked from 20 to 30 cigarettes, whereas my weekday quota was from 5 to 6. On the basis of these observations, I stopped smoking before undergoing bronchoscopic studies, which were contemplated to rule out a neoplasm. Two days after I stopped smoking, the wheezing and constriction completely disappeared. There were no further chest pains, and I have subsequently been entirely free from upper respiratory infections.

The only other reference to this condition was the description of his own case by Fogg.[3] He emphasized the obstructive sensation in the chest and rhythmic darting pains with precordial constriction. Since July, 1949, I have observed 31 patients with this syndrome, which was definitely proved to be due to smoking. All the patients were either completely cured or considerably relieved on elimination of smoking. In several instances, its resumption precipitated a recurrence of the condition.

TABLE 1.—*Incidence of Symptoms in Thirty-One Patients with Smoker's Respiratory Syndrome*

Symptoms	Intensity		Total
	Severe	Slight	
Wheezing	9	22	31
Cough and expectoration	12	19	31
Chronic pharyngitis	13	18	31
Dyspnea on exertion	4	6	10
Constriction in chest	4	20	24
Frequent, acute sore throats	22	9	31
Tendency to febrile chest colds	..	..	22
Tendency to afebrile chest colds	..	..	9
Hoarseness	5	12	17
Chest pains	5	18	23

SYMPTOMS

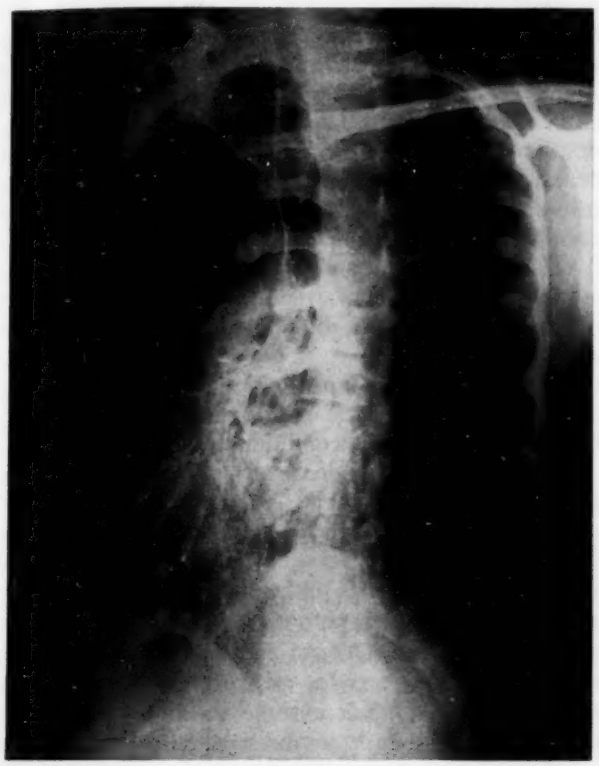
Table 1 presents a tabulation of manifestations noted in this series of patients, 20 men and 11 women from 28 to 72 years of age. Asthma-like wheezing, chronic inflammation of the pharyngeal mucosa and tonsillar area, cough, expectoration, and a tendency toward acute respiratory infections were noted in all cases. Dyspnea on exertion was present in about one-third of these patients, but it was usually not very pronounced except in one case in which it did dominate the clinical picture. Chest pains were angina-like and occurred in practically any part of the lungs, around the heart and hypogastrium and radiating into the neck and arms. Laryngoscopic examinations were made in only seven cases; Myerson's lesions of the larynx were seen in three of these.

The most constant clinical feature that suggested the diagnosis of this syndrome was chronic pharyngitis. The pharyngeal mucosa showed constant hyperemia and lymphoid hyperplasia and was often covered with mucopurulent material. The small lymphoid nodules, appearing at the pharyngeal wall, were perhaps the equivalent of the lesions described in the larynx by Myerson. Chest

1. Myerson, M. C.: Smoker's Larynx: Clinical Pathological Entity, Ann. Otol. Rhin. and Laryng. **59**: 541-546 (June) 1950.
2. Harkavy, J.: Hypersensitiveness to Tobacco and Biopsy Studies of Skin Reactions in Vascular Disease, J. Allergy **9**: 475-488 (July) 1938.
3. Fogg, A. H.: Queries and Minor Notes: Allergy to Tobacco Smoke, J. A. M. A. **144**: 810 (Oct. 28) 1950.

x-rays usually revealed an accentuation of the hilar markings but otherwise were not remarkable. Various degrees of intensity and chronicity of these symptoms were noted. In some, the condition resembled bronchiectasis, but this diagnosis could not be substantiated by bronchograms. An illustration of such an instance follows.

CASE 1.—A 32-year-old woman was seen in April, 1930. Her complaint was of persistent sore throats, shortness of breath, and marked wheezing. This had persisted practically without interruption for almost 10 years and had become severer during the past two months. She suffered from 8 to 12 respiratory infections a year. In the mornings she usually expectorated from 0.5 to 1 oz. (14.2 to 28.4 gm.) of purulent sputum. Repeatedly, she suffered sharp pains throughout the chest that were not related to respiration, heart action, or exertion. Her past history was noncontributory, except for arthritis in childhood. Skin tests performed on several occasions gave negative results. Repeated courses of antibiotics had no effect on the condition.



Bronchogram of patient described in case 2. There is no evidence of bronchiectasis.

Examination showed slight deviation of the nasal septum; the nasal mucosa was of good color; and the pharyngeal wall was markedly inflamed and covered with a mucopurulent discharge. There was moderate emphysema and wheezing throughout the lungs. The wheezing was most intense in the upper parts of the bronchial tree. There was no blood eosinophilia, and the white blood cell count ranged from 8,500 to 11,200. A roentgenogram showed accentuation of the hilar markings that were indicative of chronic bronchitis. A bronchogram revealed no evidence of bronchiectasis (see figure). Bronchoscopy revealed an inflammatory process in the trachea, larynx, and bronchi. Both stem bronchi were filled with thick, tenacious mucus exuding from the lower lobes. Examination of the secretions showed large numbers of leukocytes, no eosinophilia, and no fungus spores. The bronchoscopic diagnosis was chronic bronchitis.

The patient had been smoking between two and three packs of cigarettes daily since the age of 17. She stopped smoking completely, and within 10 days there was a remarkable improvement. Wheezing decreased, expectoration of sputum ceased completely, and the throat appeared less irritated. This improvement continued until she started to smoke from five to eight cigarettes daily and the former symptoms promptly reappeared. Smoking was stopped for a few weeks and she again improved. When she was seen by me on Oct. 21, 1950, she had resumed smoking, all the previous manifestations had developed, and she had just recovered from a severe, febrile, upper respiratory infection.

DIFFERENTIATION FROM BRONCHIAL ASTHMA

"Smoker's asthma" (smoker's respiratory syndrome) can readily be distinguished from allergic asthma (table 2). The paroxysms of wheezing are not nearly as distressing as those of allergic asthma. The patient can sleep lying down; usually, the asthmatic patient cannot. The wheezing is localized principally in the tracheobronchial region; in the asthmatic patient, it is heard anywhere in the lungs. Upper respiratory infections originate in the pharynx or tonsils; in bronchial asthma, on the other hand, the "colds" are usually localized in the mucous membranes of the nose and sinuses, which exhibit the typical allergic edema and pallor. In "smoker's asthma," these structures as a rule are not affected. In seven of our cases, vital capacity readings showed an average decrease to only 92% of normal, which is much less than in bronchial asthma. In "smoker's asthma" there is usually no allergic background and no eosinophilia in the blood and in the nasal and bronchial secretions. Skin reactions to tobacco smoke or tobacco extract are normal in "smoker's asthma" and there are no other sensitizations. However, in "smoker's asthma," exposure to such irritants as odors of paint, burning wood, frying fat, and grain dust may bring about asthma-like wheezing.

TABLE 2.—*Differentiation Between Smoker's Respiratory Syndrome and Bronchial Asthma*

Diagnostic Factors	"Smoker's Asthma"	Bronchial Asthma
Wheezing	Localized in upper parts of lungs and trachea	Anywhere in lungs
Respiratory distress	Slight	Marked
Origin of upper respiratory infections	Throat and pharynx	Nose and sinuses
Pharynx	Chronic infection	Postnasal drip
Emphysema	Slight in the 31 cases reported	Extensive
Hoarseness	Common	Rare
Eosinophilia in sputum and blood	Absent	Present
Intradermal skin reactions	Negative	Usually positive
Family and personal background of allergic reactions	Negative	Usually positive
Vital capacity	Slightly decreased (7 cases)	Usually greatly decreased

COINCIDENCE WITH BRONCHIAL ASTHMA

"Smoker's asthma" may occur in patients with allergic asthma, if they are habitual smokers. It is indeed possible to recognize the two coexisting conditions, as illustrated in the following case.

CASE 2.—A 27-year-old woman consulted me because of chronic, perennial asthmatic attacks of moderate severity. These attacks usually were aggravated at the termination of the hay fever season, in the fall, and throughout the winter. The patient also suffered frequently from severe upper respiratory

infections characterized by cough, soreness in the throat and chest, and a temperature up to 102 F. She had had bronchopneumonia on four occasions. Her tonsils were removed twice, without apparent effect on the "colds" or the constant irritation of the throat. Her history revealed a family background of allergy and particularly, ragweed hay fever in the patient. On examination, she presented typical features of allergic asthma, polyp formation and pallor of the nasal membranes, a high palate, and malposition of the teeth often encountered in asthmatic patients. At times, the sinuses were cloudy. The pharynx showed evidence of chronic inflammation. The chest showed asthmatic wheezing throughout and a moderate degree of emphysema.

When the patient was seen at home during her febrile episodes, an acute pharyngitis was always the principal manifestation. This was usually associated with expiratory wheezing in the upper portions of the bronchial tree. Skin tests were conclusively positive to all types of antigens. Intensive desensitization treatment for ragweed and other inhalants to which she was sensitive produced satisfactory local reactions; the asthmatic attacks became fully controlled; however, a slight expiratory wheeze persisted. There was a persistent swelling and soreness of the cervical glands, and there were sporadic pains in the lungs, with the sensation of choking in the throat. In recent months, there had been a slight rise in temperature on several occasions and the white blood cell count was above 10,000. The sedimentation rate was slightly increased. Repeated x-ray examinations of the chest were normal. In July, 1950, this patient gave up smoking. She had consumed between one and two packs of cigarettes daily. Within two weeks the wheezing stopped entirely and the irritation in the throat and the lymphadenitis cleared up. She has had no further asthma or any respiratory infections since then.

COMMENT

In the 31 cases on which this study is based, evidence of allergy was absent. This in itself indicates that sensitization to tobacco probably played no part in these cases of "smoker's asthma" and that the symptoms were due to chemical irritation from tobacco or other irritants. The wheezing can be explained by the fact that the mucus formed because of chronic inflammation partially obstructs the air passages. This obstructing material was actually observed on bronchoscopic examination. The presence of mucus in the air passages, as well as the action of tobacco itself, accounts for the feeling of constriction and for bronchospasm and dyspnea on exertion.

That respiratory sensitivity to tobacco exists cannot be denied. Rosen and Levy [4] reported the case of an infant who had typical asthmatic attacks, which were promptly relieved when his parents stopped smoking and were reproduced when his parents resumed smoking. This child showed positive skin reactions to tobacco and house dust. According to Pipes, between 9 and 10% of patients with respiratory allergy suffer aggravation when exposed to tobacco smoke. Positive intradermal reactions to tobacco and tobacco smoke are quite common among allergic patients; however, even in patients with 3 and 4 + reactions, no clear-cut correlation of the skin tests with asthmatic symptoms was observed. The irritating action of substances in tobacco smoke, such as nicotine, pyridine, collidine, ammonia, hydrocyanic acid, and carbon monoxide is by far more important than true sensitization. It is generally believed that the mucous membranes of some persons manifest a greater tolerance to these irritants than those of other persons.

Several years ago I observed a patient in whom violent sneezing spells developed when she was exposed to the smoke of one particular brand of cigarette. When I voiced skepticism, she asked to have someone in the waiting room light a cigarette while she remained in my office about 30 ft. away. Several cigarettes were lighted with no effect, but the patient reacted immediately when the particular brand to which she was sensitive was lighted. Unfortunately, I was unable to carry out further investigation in this case because the maker of the particular cigarette was unwilling to name the ingredients that might have been responsible.

I believe that the "smoker's asthma" syndrome described above is not rare, although its relation to smoking is not always easy to prove. Often when told that smoking is the source of their disease, patients may not return for further studies because they refuse to give up smoking. In the majority of patients, the pharyngitis and other symptoms disappear promptly on elimination of smoking, although, in some patients irreversible lesions undoubtedly develop as a result of the persistent irritation and frequent infections. Under my care are several persons who have more advanced, probably permanent, changes for which smoking is suspected as the sole cause. These patients were not included in this series, because it is impossible to establish a clear relationship to smoking, since its elimination does not clear up the condition. One can only speculate on the possibility that so-called idiopathic emphysema or "intrinsic asthma" and bronchiectasis of unknown etiology might be the end result of the condition described here.

In the diagnostic aspects of "smoker's asthma," it should be emphasized that in some of my patients the diagnosis of bronchiectasis was based on the large amounts of material expectorated in the morning and on the physical findings. Others went through intensive allergic management before the condition could be properly evaluated. Others, like the patient in case 2, were treated for years for an existing allergic disease, yet the source of their chronic condition went undetected. Recognition of "smoker's asthma" is therefore of paramount importance. In the treatment of this syndrome, complete elimination of smoking is the method of choice. Antibiotic therapy may be suggested in more advanced cases.

SUMMARY

A clinical syndrome characterized by dyspnea wheezing, constriction in the throat and upper air passages, and pain in the chest associated with a tendency to frequent upper respiratory infections is described. It was observed in 31 patients; 25 sought treatment for asthma and 6 had been suspected to have bronchiectasis. This asthma-like condition is induced by smoking and subsides on elimination of smoking. It is also discussed in connection with allergic asthma. It is possible that this condition may contribute to the development of permanent pulmonary changes, such as chronic emphysema, bronchiectasis, and so-called intrinsic asthma, in which the etiological relationship cannot be established.

602-604 Professional Bldg. (1).

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CHILDREN'S SHOES

Louis Starr, M.D., Brooklyn

The subject of children's shoes is best covered by answering in some detail the questions usually asked of the physician by the parents. Certain fundamentals about the foot and footgear must be considered first.

1. Shoes are essentially articles of clothing. They are protective; the entire shoe protects against the influence of weather, and the sole and heel protects against rough surfaces, thorns and pebbles, and hard pavement surfaces.

2. The normal foot requires no support from shoes. The shoe, therefore, should be pliable and interfere as little as possible with the action of the foot.

3. A weak foot is a foot that on weight-bearing changes its shape and contour more than normal. The longitudinal arch rolls inward and flattens, hence the term flat foot. The heel and Achilles tendon tilt outwards, hence the term pronated foot or valgus foot. The inner border of the foot bulges. The inner malleolus at the ankle becomes more prominent, hence the term ankle valgus or double ankles. The accepted orthopedic treatment is to support such a foot throughout the growth period of childhood. This can be accomplished by shoes, by shoe modifications, and by various types of inserts usually called arch supports.

4. A proper shoe fit is essential for foot health. Poorly fitting shoes are uncomfortable. They wear out more rapidly. They may result in deformities of the foot.

SHOES FOR INFANTS

The first question parents usually ask is "When should my infant start to wear shoes?" An infant's foot needs no protection while the infant is in the crib or playpen. Protection is desirable as soon as the infant maneuvers about to any considerable extent outside the playpen. The diagnosis of weak foot can be made as soon as the infant on suspension bears some weight on its feet. Standing with the toes pointing out more than 45 degrees is invariably associated with a weak foot. A weak foot requires support, and the wearing of adequate shoes is imperative as soon as the infant is able to draw himself up into the standing position.

Parents also ask, "Should my infant have low or high shoes?" One of the advantages of high shoes is that they can be maintained on the foot more easily than low shoes. This is particularly important in an infant, who resents shoes the first time they are applied and who will try to kick them off if he can. With low shoes this would be fairly easy, and the mother would be continuously reapplying the shoes. Actually, low shoes are often difficult to obtain in the sizes for an infant who is learning to stand and walk. The answer to a parent is, therefore, high shoes.

Later parents may ask, "Should my child have low or high shoes?" The answer to a parent is that the child should have low shoes. They are cooler, dryer, and afford adequate protection for the foot. The same answer also holds for children with weak feet. The primary deformity in weak foot occurs below the level of the ankle. The thin extension of leather upwards in high shoes covers the malleoli and can hardly be expected to prevent the foot from flattening under the stress of body weight merely by hindering the increasing prominence of the inner malleoli. High shoes do serve a psychological function in that they hide what is going on in a weak foot. The deformity of the weak foot is much more visible in a low shoe, especially the inflare at the ankle and the outflare at the heel.

BUYING CHILDREN'S SHOES

Many parents ask, "What brand of shoe should I get?" There is no standard reply. The shapes of children's shoes are so well standardized that their shape is usually correct. Shoes are made over lasts. A last is a reproduction, generally of maple wood, of the approximate shape of a human foot. A standard or normal last is one in which a set of standard measurements are used throughout, namely, standard length, standard width, standard instep, standard heel, and standard ankle. This kind of last is scientifically designed to fit an average foot. There is no distinction between the lasts made for the manufacturer of high grade footwear and those produced for use in making inexpensive shoes. Not all manufacturers, however, make shoes in all of the available lengths and widths of standard lasts. The less expensive the shoe the more the tendency to concentrate on the most popular sizes. The more expensive the shoe the greater the available range. In fact, in better grade shoes, combination lasts are often available, that is, shoes made on lasts with variations from the standard measurements. Feet differ so much from each other that a proper fit is better insured if there is a wide choice of sizes, lengths, widths, and lasts available.

The choice of the store at which the parent should buy the shoes is determined to a minor extent by the brand of shoes sold and to a major extent by the reputation of the store in the community, as determined by the reports of patients regarding the service and the salesman and by the physician's own personal observations and experience. A full range of sizes—lengths and widths—must be kept in stock or be readily available.

Shoes should not be bought from a mail-order house or off the counter. A good fit is difficult to obtain in this way. A shoe store should not have a fluoroscope. No regulations can make shoe fluoroscopy safe. A competent shoe salesman can achieve a good fit without resorting to shoe fluoroscopy.

The salesman in the store is all important. He must be experienced, and he must know his stock. Even standard lasts vary from model to model, and a child may be best fitted with a size 6C in one last and a size 6B in another last. A salesman must be able to give as much time as may be necessary to do a good fitting job.

If the salesman tells the mother at any time that he is giving the child a pair of shoes a little too large and

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that the child will grow into them, that salesman is interested in making a sale, not in correctly fitting the foot. If the salesman tells the mother at times that the child's shoes still fit and that new shoes are not necessary, that salesman is interested in giving the correct fit. Some stores make it a practice of telling a mother to return at intervals to check on whether the child has outgrown his shoes. Children frequently outgrow rather than outwear their shoes.

Parents often say to the physician, "Does my child need new shoes now? He's had them for some time." Children's feet often grow in spurts, and the fact that a child has had a pair of shoes for four or five months does not mean that he needs a larger size. The best test is to note the distance between the tip of the first and second toe from the end of the shoe while the child stands. This is usually done quite easily as the toe box has lost some of its stiffness. In the event of any difficulty, the child can be instructed to wiggle his toes. Shoes are outgrown when this distance is ¼ in. (0.6 cm.) or less. At times shoes are worn out before they are outgrown. If the linings are badly torn, repairs are undesirable and new shoes should be obtained.

THE FIT OF SHOES

Parents may ask whether shoes just obtained are properly fitted. The procedure for checking the fit of shoes is simple, and no special instruments are necessary. Both shoes should be put on the child and laced firmly. The child should stand with full weight borne equally on both his feet. The following points should be determined:

1. The position of the eyelets should be noted. They should be parallel. 2. The heel to toe length measurement should be determined. The tip of the big toe and second toe should be felt through the upper. Sharkskin tips of children's shoes make this difficult to do when the shoes are new. The distance between the toes and the tip of the shoe should be ½ in. to ¾ in. (1.2 to 1.9 cm.) (the width of an adult's thumb). If this is not possible, an outline of the weight-bearing foot can be traced later and checked against the shoe. 3. The heel to ball length should be checked. The widest part of the child's foot, the region of the metatarsophalangeal joints of the big and small toes, should be at the widest part of the shoe. The ball of the foot and the ball of the shoe should meet at the same point, so that the foot and shoe may bend at the same place. 4. The width across the ball of the foot should be noted. It should be possible to grasp a small fold of leather across the front of the vamp with the thumb and forefinger. If the leather wrinkles, the shoe is too wide. If it seems tense and bulging, the shoe is too narrow. 5. A shoe should fit in action as well as at rest. When the child raises his heel and bends forward so that the weight of the body is on his toes, the shoe should not gape at the sides or at the back. 6. The child should walk around for several minutes. The back of the shoes should fit snugly without slipping or riding up and down, and they should be comfortable.

Many parents wonder, "How can I be sure that my child's shoes are well-fitted?" The integrity of the store and the experience of the salesman are the deciding factors, but some additional advice to parents may be in order. If at all possible shopping should be done during lull hours when neither the parent nor the fitter is hurried. Shoes should not be bought by size. In different makes or lasts, a foot may require different sizes. Once a fitter is found who knows his business, he should continue to fit the child's shoes.

I have tried to show mothers how to check the fit, but most of them would rather not have the responsibility. In actual practice the best policy often is to tell a parent to bring the youngster to the office for the physician to check the fit of the shoes.

OTHER QUESTIONS

It can be determined whether the child is wearing out his shoes normally by checking the worn areas on the shoes. The striking surface of the heel is the outer back corner, and this is the part of the shoe that usually wears out first. Only part of the sole bears the weight, the part under the metatarsophalangeal joints. This broad band, 1 in. (2.5 cm.) or more wide, shows wear, although often wear is most marked under the ball of the big toe where push-off occurs.

The tip of the sole may show signs of excessive wear, especially when there has been considerable running and when in riding a tricycle the shoe has been pressed against the ground and used as a brake. Shoes that are too short may result in flexion of the toes in an attempt to shorten the length of the foot. This may be associated with signs of excessive wear at the tip of the sole.

Sometimes parents ask whether steel taps can be put on the soles or heels. A metal insert tends to prevent too rapid wear. It is often used on the outer back corner of the heel and occasionally on the tip of the sole. It has disadvantages; it increases the tendency to a clicking sound when the heel strikes hard surfaces, is slippery, and may tend to cause the child to fall.

Parents often ask whether the child needs two pairs of shoes. The answer is that they are not necessary, but they are extremely desirable. When worn on alternate days, the shoes will dry out more completely. It is not at all wise to use hand-me-downs, as it is impossible to obtain a good fit in this manner.

Another point of concern for parents is whether the child should be permitted to walk barefoot. In the house barefoot walking should be at a minimum. The foot even needs protection in the house against occasional pins, needles, and other objects on the floor. Barefoot walking should be prohibited if any person in the house has athlete's foot (dermatophytosis). A child may be allowed to walk barefoot in the sand or on grass. This is excellent exercise for foot and toe muscles.

A related question is whether the child should wear slippers. They are a convenient hygienic measure provided they are limited to the use for which they are intended. They should not be used just because the child is in the house, for example, on a rainy day. They should not be used when the child is allowed up and about the house during convalescence from an illness that has kept the child in bed for days or weeks.

Sneakers are another type of footgear that parents ask about. Sneakers must offer adequate protection of the sole and heel against hard pavements. The running and jumping indulged in by the child necessitates a thick rubber sole as a shock absorber to protect the soft tissues of the heel and sole. The rubber soles of some sneakers do not offer such protection. The canvas of sneakers must be porous to allow adequate evaporation of the perspiration. Even so, frequent changes of socks and free use of foot powder are advisable. Often the design of a sneaker is faulty; the toe area is usually too pointed, resulting in pressure on the toes. Sneakers are very flexible and are ideal for athletic activities such as in the gymnasium and on the tennis court. They are not intended for use all through the day, and they are not intended to replace shoes. They may be worn for limited periods of time when the child is indulging in some athletic pursuit.

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CLINICAL NOTES

BILATERAL OPTIC NEURITIS FOLLOWING CHLORAMPHENICOL THERAPY

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and
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Bilateral optic neuritis caused by chloramphenicol (chloromycetin®) is unusual. A thorough search of the literature, which is increasingly revealing the toxic manifestations of this antibiotic, has uncovered only one other similar instance.[1] The aromatic amines are capable of depressing bone marrow function. Organic compounds that have a benzol ring with an attached amino or nitro group and that are readily oxidizable can depress the bone marrow function. Chloramphenicol contains such a group. Being rapidly absorbed from the gastrointestinal tract, it appears promptly in the blood stream after ingestion; the concentration in the cerebrospinal fluid is about half that in the blood. It is excreted in the urine in high concentration, about 10% being in the active form. It is primarily excreted through the kidneys, with 90% of the administered dose accounted for in 24 hours.

Numerous cases of severe aplastic anemia following chloramphenicol therapy have been reported in the literature. In addition to the hematopoietic effects, other types of toxicity have been observed, such as anaphylactic reactions, cutaneous eruptions, mucous membrane irritations, and psychiatric disturbances. The following case has been of great interest to the authors because of severe involvement, with partial recovery, of the optic nerves.

REPORT OF A CASE

J. G., at the age of 14, had an attack of acute rheumatic fever, which left him with a cardiac murmur. This was symptomless and entirely nonincapacitating. He was inducted into the armed forces in 1943 and discharged in 1945. The cardiac murmurs were noted on induction and discharge physical examinations. He was apparently well until Nov. 16, 1951, when he was suddenly seized by chills and fever, with temperature rises to 105 F. On the fifth hospital day, petechiae of the skin and conjunctivas and small hemorrhages under the nails developed. The spleen was found to be palpably enlarged. Blood cultures were taken and were reported positive for hemolytic Staphylococcus aureus. A diagnosis of a bacterial endocarditis was made. These bacteria were found to be sensitive to chloramphenicol and completely resistant to penicillin. The patient was given 6 gm. of chloramphenicol daily. After five weeks, he was transferred to the Brooklyn Veterans Administration Hospital, where he continued to receive 6 gm. of chloramphenicol daily for a few days. On the sixth day after the original institution of chloramphenicol therapy he became afebrile and remained so. Blood cultures became negative and remained negative after the course of chloramphenicol therapy.

At the first hospital, a severe anemia was noted, and the patient was given two units of whole blood. A mild urticarial reaction, with a slight rise in temperature, followed this treatment. On admission to the Brooklyn Veterans Administration Hospital, results of a blood examination were as follows: red blood cells, 3 million; hemoglobin, 8 gm. per 100 cc. (Sheard and Sanford); white blood cells, 4,600, with a normal differential count. This anemia gradually disappeared with the discontinuance of chloramphenicol.

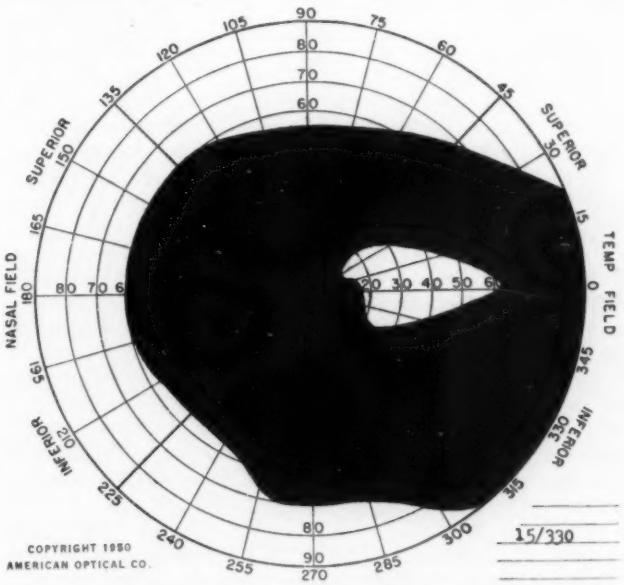

Fig. 1.—Results of perimetric examination of the right eye done April 30, 1952.

The day after the completion of the six week course of chloramphenicol, the patient complained of cloudy vision and, on awakening the following day, found he could not see at all. Examination of the eyes at that time revealed no external pathological condition. The ocular movements were normal. The pupils were widely dilated, round, and fixed. There was no response to light. The media were clear. Both optic disks appeared pale and slightly edematous; the nasal, inferior, and superior borders were indistinct; only the temporal margins were visible. This seemed to be more pronounced in the right eye. In the right fundus, a large triangular hemorrhage was noted to impinge on the upper nasal portion of the optic disc,

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Reviewed in the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

1. Wallenstein, L., and Snyder, J.: Neurotoxic Reaction to Chloromycetin, Ann. Int. Med. 36:1526-1528, 1952.

with a large puffball hemorrhage immediately superior to the disk. The macula was dull in appearance. In the left fundus, there was a massive preretinal macular hemorrhage, with a large hazy green-gray mass with indistinct margins in the upper portion of this hemorrhage. Smaller scattered hemorrhages were noted in various parts of the fundus. The arteries appeared to be normal in caliber, whereas the veins were mildly dilated.

With the onset of the visual difficulty, acne-like lesions were noted about the face and forehead. The neurological examination revealed no abnormalities. The spinal fluid was under normal pressure, clear, and had normal constituents (two white blood cells, a normal globulin level, and a slightly elevated total protein level), and results of a serologic test for syphilis were normal.

As the edema of the disks decreased, there was a corresponding increase in optic disk pallor. The hemorrhages were gradually absorbed. The left preretinal macular hemorrhage gradually changed to an elongated gray-white exudate, which was eventually absorbed, leaving small dull gray exudates in the inferior and temporal region of the left macula. With the gradual restoration of the fundi to a more normal status, the pupillary reflexes as well as some vision were restored. The visual acuity at the last examination was as follows: right eye,

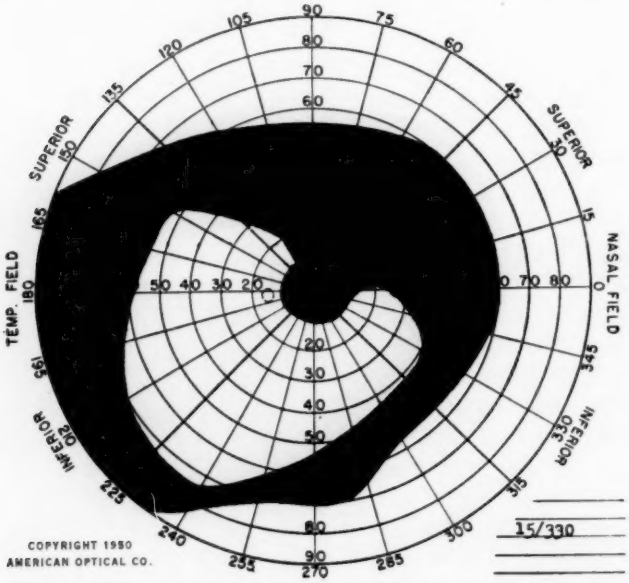

Fig. 2.—Results of perimetric examination of the left eye done April 30, 1952.

fingers at 2 ft.; left eye, 20/200. The perimetric examination revealed an arrow-head profile of vision in the midtemporal field of the right eye; an absolute central scotoma, which spread superiorly into a funnel-like defect, with general peripheral contractions, was noted in the left eye (fig. 1 and 2).

SUMMARY

A patient with an acute exacerbation of a bacterial endocarditis was given 6 gm. of chloramphenicol (chloromycetin®) daily for six weeks. During and on completion of this therapy the following complications developed: (1) severe anemia, (2) cutaneous manifestations (acne-like lesions), and (3) bilateral optic neuritis. The anemia and the cutaneous manifestations gradually returned to normal with cessation of therapy, but the visual difficulties did not resolve themselves. The vision, as well as the visual fields, has remained seriously affected.

1 Nevins St. (17) (Dr. Lasky).

COUNCIL ON FOODS AND NUTRITION

The following report was prepared at the request of the Council on Foods and Nutrition.

JAMES R. WILSON, M.D., *Secretary.*

DISASTER FEEDING

James M. Hundley, M.D., Bethesda, Md.

Natural disasters are not strangers to this country. Many people have been killed or injured and thousands have become temporarily homeless as a result of fire, flood, windstorm or earthquake. Various organizations, especially the Red Cross, have had extensive experience in feeding and otherwise caring for people under such conditions. Man-made disasters such as an enemy could inflict on this country today represent an experience which the American people have not yet had to endure. Likewise, no American organization has had experience in meeting this type of disaster. The physical, medical and psychological problems posed by atomic, biological or chemical warfare, or even massed conventional and fire bombing are of a type and magnitude which demand special thought, planning and organization if they are to be met successfully. It is such considerations which led to the establishment of a Civil Defense organization in the United States.

A vital part of every Civil Defense plan must be for disaster feeding. The prompt provision of warm food and drink for the injured and homeless is a must if morale is to be maintained, panic avoided and the stricken community restored to a functional state in a minimum of time. As this communication will attempt to show, disaster feeding is important for reasons other than just to give nourishment to those who cannot provide for themselves. It is an effective means of therapy, a tool for mass therapy, which should rank in importance with the medical treatment of the injured. Indeed, it is an important factor in such treatment.

THE HOMELESS

This term is used to refer to those whose homes have been destroyed or rendered uninhabitable and who have not suffered injury sufficient to require hospital care. The need for emergency (disaster) feeding of this group can be examined from two viewpoints, physiological and psychological.

Physiological Factors.—As is well known, a lack of drinking water will produce death far more quickly than a complete lack of food. For this reason a high priority should be given to the provision of an emergency supply of potable water. It is well established that adults, previously well nourished, can withstand many days of fasting without harm.[1] They can even maintain moderate activity at the expense of some loss in body weight. Numerous human fasts of 20 to 40 days have been recorded. The subjects recovered from these fasts with no detectable permanent damage. With proper psychological motivation individuals under normal circumstances can maintain a calm and intelligent adjustment to a temporary lack of food and continue some useful activity.

Psychological Factors.—The pertinent point is that the homeless under disaster conditions are not in a psychologically well-adjusted state. They have been through a very distressing experience. Their homes, belongings and loved ones may have been lost. A bombed population, especially in the first

Because of lack of space, the bibliographic references have been omitted from THE JOURNAL and will appear in the author's reprints.

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few hours, seems to suffer a type of emotional shock which results in a dazed condition with an impairment in the normal capacity to reason. The real or imagined use of atomic, biological or chemical weapons would add a further emotional stress. Here are potentially lethal agents in their environment with which they have had no experience, which they are not sure they could recognize if present, nor sure that they could combat if recognized. These are the basic elements of panic and disordered flight.

Ross [2] has published a careful study of his psychiatric analysis of available data on the reactions of individuals in disasters, including the Hiroshima atomic explosion. He divides the reactions into three phases: (1) the period of impact; (2) the period of recoil; and (3) the post-traumatic period, during which most persons return essentially to normal, although a few develop traumatic neuroses. The period of impact corresponds to the duration of the direct initial stress or emergency. Individuals can be divided into three groups according to their reactions during this period: (1) the minority, 10 to 25% who are in full possession of their faculties; (2) the majority, about 75%, who show some inadequacies in their reactions, such as restriction of attention or physiological signs of fear and reflex behavior; and (3) the remainder, 10 to 25%, who are grossly incapacitated by emotional disorganization. The second phase, the period of recoil, involves a gradual return of self-consciousness and awareness for the majority. Feelings of anxiety, fear and anger develop. Attention is directed to finding relatives, seeking shelter or care. It is during this period that individuals can be influenced in their recovery toward normal. Some manifest a need to talk to someone. Many can be favorably influenced by giving them a blanket or a cup of coffee to convey a feeling that they will be looked after.

It is at this stage that adequate emergency feeding arrangements can exert a telling influence in helping people back to normal. This is the keystone of the entire program for the adjustment period—helping people so that they can help themselves. A cup of coffee or warm food from a functioning emergency feeding group constitutes tangible proof that the community is still functioning, that others are not fleeing in panic and that doomsday has not yet arrived. As a matter of fact, those doing the emergency feeding are helped themselves since preoccupation with helping others is one of the best defenses against anxiety and aids these workers in eliminating their own terror. It should be emphasized that the immense practical importance of prompt, adequate emergency feeding is based not on theory but on experience and demonstrated fact. Organizations, such as the Red Cross, through long experience with natural disasters in this country, make every effort to get their canteens into operation at the earliest moment, even if to provide only coffee and doughnuts in the initial phase. During World War II the Germans made a practice of supplying extra food to bombed areas and had their food stocks so organized that they could move food into a bombed area within 1½ hours after an attack.[3] Their emergency feeding scheme was so organized that 1,200,000 people were receiving emergency meals within 48 hours after the saturation bombing attacks on Hamburg and environs were begun. The prolonged bombing of Great Britain, especially during the heavy raids on London from September, 1940, to May, 1941, and the mass raids on Coventry and Sheffield in November and December, 1940, quickly demonstrated the importance and necessity for emergency feeding as well as other mass care facilities, in averting panic and in maintaining the will to win.[4] It is worthy of note that Great Britain, on the basis of its experience during World War II, is making careful, detailed and elaborate plans for emergency feeding during a potential future conflict.[3] Furthermore, the British continue with the procurement of equipment and the pursuit of training activities on a scale far beyond anything yet in progress in this country.

The analysis of psychological factors outlined is based largely on individual reaction patterns and on such disaster experience as has already been experienced and evaluated. More modern forms of mass destruction pose a real problem of mass hysteria. Actually, there is no experience, American at least, on which to base a concrete judgment as to the likelihood or probable magnitude of mob reactions nor is expert opinion agreed on this point.[5] However, it is certainly pertinent to note that the reactions of masses are but the peculiarly and unpredictably catalyzed sum of individual reactions. Therefore, the extent to which individual reactions can be normalized will heavily influence any tendency to mass hysteria. Experience in Great Britain during World War II clearly demonstrated that mass reactions to heavy bombing could not be controlled by police action alone. Thus, emergency feeding assumes added importance in situations where mass hysteria might be expected.

Nutritional Factors In Feeding the Homeless.—From the foregoing, it is obvious that the primary consideration in feeding this group is psychological rather than physiological. It does not follow, however, that feeding plans can be haphazard. "Any old food" will not do. There are certain principles and policies which must be observed in successful emergency feeding. The first need in the hours immediately after the disaster is for a cup of good stimulating beverage. With most adult Americans this would be a cup of hot, not lukewarm, coffee. Infants and children should be provided with milk not only for their own benefit but to calm the anxiety of parents.

The food served should be primarily designed to allay hunger and sustain morale rather than to fit any rigid nutrition standard. Under the conditions of the usual type of disaster, and according to the general Civil Defense plan, it is unlikely that any one individual will be dependent on emergency feeding for longer than 7 days and in no instance longer than 30 days. Specific nutritional deficiencies will not develop in previously well-nourished individuals within this time. Even those marginally nourished should suffer no ill-effects if the foods used are primarily natural, normal foods whose composition is as varied as circumstances will permit. It follows then that calories are the predominant nutritional consideration in feeding this group. The Federal Civil Defense Administration has recommended,[6] for planning purposes, a daily per capita calorie allowance of 2,000-2,200 which will provide adequately for a population of normal age-sex distribution and properly rationed, will allow some margin of safety to provide for the higher allowances needed by special groups (*vide infra*). Detailed consideration of individual nutrients need not be undertaken. Most state and local Civil Defense organizations have followed this general pattern as to calories and nutrients, although one, at least, has also set recommended standards for protein and for vitamin B_1.[7] The necessity for such detailed planning has been questioned by the Food and Nutrition Board of the National Research Council,[8] and it does needlessly complicate the planning and organization of emergency feeding arrangements.

It is obvious that should a real disaster strike, such food as can be procured will be prepared and served as generously as possible in the age-old American tradition. It is important, however, to have some nutrition standard for emergency feeding for purposes of training, for planning of menus and recipes, for estimating the probable adequacy of locally available supplies, for allocation of available supplies and for reassuring the fearful that the food they receive at emergency centers will be adequate to protect their health. The foods provided for emergency feeding should be familiar, well-liked foods with a high general acceptability. The importance of this cannot be over-emphasized. People in disasters are in a state of stress. Stressed individuals tend to reject unliked or unfamiliar food much more readily than they would under normal circumstances. As noted by Drummond,[9] the half-starved people of Malta during World War II threw dried eggs into the street rather than eat an unfamiliar food. Rice-eating Hindus in the great famine died before they would touch the millet which relief brought. British troops "wore themselves to skin and bone" in the Burmese jungle rather than endure the monotony of living exclusively on the famous K ration, one of the most scientifically compounded of all the wartime

rations. Magee [8] noted that the people of Berlin, during the Berlin Blockade of 1948-1949, rejected the monotony of dried beef even though they were malnourished and their diet was low in animal protein.[10] It soon had to be replaced by other more acceptable food. These facts rule out the use of many bizarre and unfamiliar specially designed food preparations which have been proposed for Civil Defense emergency use. This situation has been discussed more thoroughly elsewhere.[11]

The physician, within the usual framework of Civil Defense organizations, is involved or affected by the plans for this group in three ways. The adequacy or inadequacy of the emergency feeding program for the homeless will certainly influence the number of casualties the physician will be called on to treat. Adequate feeding will aid in preventing post-traumatic neurosis, tend to reduce the numerous injuries inherent in any mass panic reaction, and assist the afflicted population to a maximum of self-help.

Secondly, the plans for most Civil Defense units provide that the same groups which will be responsible for the procurement, distribution, preparation and serving of food for the homeless will also be responsible for providing necessary food to emergency hospitals and in some instances for the preparation and distribution of food within these centers of medical care. It therefore behooves the physician to carefully examine the adequacy of the preparations for emergency feeding so that the needs of his patients as well as the rest of the community can be met.

Thirdly, those patients suffering from diseases such as peptic ulcer or diabetes, whose normal therapy is in part by special diets, may have difficulty in procuring the types and amounts of food they normally require. The adequacy of the emergency feeding arrangement will determine whether they can temporarily meet their needs by diet or whether they will have to depend on medications and thus constitute an additional load on already overburdened medical resources. This will be considered more fully in a later section.

CASUALTIES

In addition to the homeless, the numerous casualties which must be expected in disasters will constitute an emergency feeding problem. While no exact estimates can be given, it is certain that casualties will constitute a very large group if one of our major cities is attacked intensively with modern weapons.[12] In particular, if high explosives, incendiary or atomic weapons are used, many thousands with burns, fractures, other mechanical injuries and, with the latter type of weapon, radiation injury must be anticipated. In addition, there will be many with major illness or injury developed prior to the attack who will have to remain hospitalized even in disaster situations.

Feeding these individuals must be viewed in a different light from feeding the homeless. Different plans are required. In the first place, the feeding must be done in medical installations—temporary or permanent. The feeding arrangements must be under medical control, usually on an individual patient basis. Diet constitutes a standard and important part of therapy for the usual hospitalized patient. In so far as possible this should be true in an emergency as it is in normal practice. The feeding problems among the casualties will vary. There will be some patients who should not be fed at all. For example, patients with gastrointestinal injury might be harmed by attempts at feeding. There will be others who should receive nourishment at any cost, by tube or intravenous feeding if necessary, to prevent nutritional depletion prior to or in preparation for major surgery. There will be the numerous patients with burns where problems of maintaining fluid, protein and mineral balance are encountered.

It is difficult on the basis of presently available evidence to be certain of the general recommendations which should be followed in the nutritional management of casualties in disaster. Opinion in the United States and in Great Britain differs sharply on this point. It is widely held in this country that the prompt provision of high caloric, high protein, high vitamin nourishment constitutes an important factor in recovery from major trauma such as burns, fractures, other mechanical injuries and perhaps even from radiation injury.[13] The technical basis for this concept and the dietary practices required to implement it in combat troops have been discussed in a special report, "Therapeutic Nutrition," from the Food and Nutrition Board of the National Research Council to our military authorities.[13a] Special aspects of this situation have been reviewed elsewhere,[14] and the special nutritional problems in burns has been considered in another report from the National Research Council.[15]

If these principles of intensive nutritional therapy are important in treating combat casualties, then they should be equally applicable in the treatment of similar injuries in civilians. In this connection, it should be noted that Goodhart and Jolliffe [7] have followed this concept in their consideration of principles of emergency feeding for a large metropolitan area in catastrophe. They also list several simple formulas which can be used as diet supplements to supply particularly the high protein part of this regimen. It is not the purpose of this review to examine the evidence for or against this system of therapy except to make the following observations. It is certainly true that major trauma results in serious metabolic upsets, in extensive breakdown in tissue protein, in striking derangements of vitamin metabolism, especially ascorbic acid, and in other changes which might be expected to result in acute malnutrition and actually resembles malnutrition in many ways. It is true that malnourished patients are usually poor risks when afflicted with disease or trauma. General experience has led surgeons to pay intimate attention to the preoperative and postoperative nourishment of their patients in attaining minimum mortality and speedy convalescence. One might expect then that intensive nutritional therapy might reverse or overcome these degradative metabolic phenomena following trauma and that this would have a most beneficial effect in aiding survival and promoting convalescence. Indeed, it has been shown that intensive nutritional therapy can overcome partially or completely the observable biochemical abnormalities. However, the crux of the entire situation in Civil Defense is whether such casualties, previously well nourished, are more likely to survive and recover at a faster rate when treated by intensive nutritional therapy. There seems to be room for a real and honest difference of opinion on this point in view of currently available evidence.[16] Intensive research is being conducted on this important point and some clarification should be available in the near future.

In contrast to the recommendations given in "Therapeutic Nutrition" [13a] the British, based on their extensive experience in World War II, are inclined to attribute little importance to intensive nutritional therapy in such conditions and they do not practice it.[17] One cannot dismiss lightly such a contrary view based as it is on the extensive disaster experience of a group of very competent scientists, no more than one can disregard the carefully considered views of the distinguished group of scientists who prepared the "Therapeutic Nutrition" report. If valid, nutrition practices following the recommendation of the "Therapeutic Nutrition" report would exert a tremendous influence in combating the effects of enemy attack. If not valid, such practices would needlessly complicate an already very complicated situation in which medical and other resources are already strained.

It is the purpose of this discussion to focus attention on two points, first, the existence and potential importance of the "Therapeutic Nutrition" concept and, secondly, to recommend a course of action to physicians who will have Civil Defense responsibilities. Certainly the medical division of each Civil Defense unit is under an inescapable obligation to examine the available evidence on this subject. In the light of this and their own experience, definite principles of nutritional treatment should be adopted. This must be done in advance and is of importance not only in training those who may be called on to administer the therapy, but in estimating the adequacy of the supply of special food items such as milk, dry milk powders, eggs, dried eggs, vitamin supplements and solutions for intravenous feeding.

Dr. Norman Wright of the British Ministry of Food has said "A sudden emergency is no time for introducing novelties" (for feeding the homeless).[18] In my opinion, this philosophy should be extended to the treatment of casualties following an enemy attack. Whatever principles of therapy are adopted, they should be those in which the medical group has confidence and experience in their use and usefulness.

OTHER SPECIAL GROUPS

Infants.—Infants, and to a lesser extent, children and pregnant and lactating women constitute exceptions to the principles discussed previously for feeding the homeless. Their nutritional needs are higher and more exacting. Infants under 1 year are particularly vulnerable to even a temporary interruption in their supply of food. Planning to meet the special needs of this group is largely a matter of assuring an adequate supply of some type of fluid milk or acceptable milk product and instituting a scheme of rationing to those with the greatest need if the supply is temporarily limited. Needs for food products other than milk can be met from the rations available for feeding the homeless. Vitamin supplements, even vitamin C, need not be provided during these short periods (maximum of 30 days). The needs of this special group and a scheme for the distribution of limited milk supplies have been discussed in detail elsewhere.[19]

Patients with Chronic Illness.—Patients with peptic ulcer, tuberculosis and diabetes constitute the majority in this category who are frequently dependent on special diets. The provision of special diets for such patients would undoubtedly be impossible in the first days following a disaster. For those so severely ill that they would have to remain hospitalized even after a disaster, temporary control of the disease would be maintained by medications plus such of the hospital menu as they could utilize.

Ambulatory but homeless patients with peptic ulcer could temporarily maintain control of their disease by medication and thus reduce the burden on both the emergency feeding and the emergency medical facilities. To do this such patients should maintain at all times at least a seven day supply of their usual medications. The usual ambulatory patient with tuberculosis would probably be damaged little, if any, by subsisting for a few days on the rations available for the homeless.

Diabetics constitute a special problem in disaster situations. The homeless diabetic would probably be unable to procure his usual diet from the simple and limited rations available. Consequently it would seem wise to place primary dependence on insulin and a thorough self-treatment education of each patient. This would mean that each diabetic should maintain a reserve stock of insulin and extra syringes and needles to administer it. Diabetics who are injured also pose special problems. Knowledge as to the existence of the diabetes could be quite important particularly in those with burns or wounds likely to become infected. The unconscious injured diabetic is an obvious problem. These considerations have led to various proposals for identifying the diabetic by a card or identification tag of some sort which would be carried at all times. The problem of diabetics under emergency conditions has been carefully and comprehensively considered by the American Diabetes Association.[20] Butler [14c] has reviewed the special problems of diabetics in disasters as well as many other special mediconutritional problems in disaster situations.

Essential Workers.—Those engaged in essential operations demanding a high level of physical output under difficult conditions should receive special rations. This includes fire fighters, those engaged in rescue operations or in maintaining or repairing essential utilities and medical personnel. It is important to feed such individuals a diet as normal as possible not only to maintain morale but to sustain them at a high level of work performance. A planning standard of at least 3,500 calories per capita daily for these workers has been recommended.[6]

FEEDING IN PROLONGED EMERGENCIES

Under conditions of actual war or in prolonged national emergencies, experience has shown that it is necessary frequently to institute rationing schemes to distribute limited supplies of food more equitably. This is, in a sense, "disaster feeding" just as the short-term emergency situations referred to in the previous discussion. The problems involved are, however, entirely different.

Fortunately, this country has never had to endure really stringent rationing. During World War II, the amount of food available per capita even with rationing was greater than before the war. It is the fervent hope of all that we will never have to endure really stringent rationing. Nevertheless, the possibility must be faced that in future conflict our food supplies may be severely limited as a result of poor crops or the necessity of contributing a substantial portion of our food to support our allies. Under these conditions, the food available domestically may be curtailed to the point where rationing would be necessary to insure equitable distribution and to maintain sufficient reserves to meet short-term disaster needs and other contingencies. It is important, therefore, that we should be prepared with realistic nutrition standards which can be applied according to the situation in which we find ourselves.

Nutrition standards for prolonged emergencies, i. e., months to years, must be considered in much more detail than the short-term disaster feeding allowances already discussed. Specific nutritional deficiencies will develop, morale and work output will decline during these longer periods if the diet is quantitatively or qualitatively inadequate. Many factors such as average age, body size, environmental temperature, the initial nutritional state of the population, the expected length of the emergency period, the level of work output expected and morale factors all exert an influence on caloric and nutrient requirements.

The one generally accepted reference standard in this country is the 1948 Recommended Dietary Allowances of the Food and Nutrition Board of the National Research Council.[21] These recommended allowances are designed for normal times and reflect nutrition "goals." They were designed to maintain and promote maximum productivity through generations. In the case of many nutrients, these allowances contain deliberate surpluses to provide for those in the population whose requirements may be above average. These recommended allowances reflect a philosophy of nutrition which is undoubtedly desirable in time of peace and plenty but which may represent a luxury we cannot afford in time of war or national emergency.

These facts are well known to the Food and Nutrition Board and at various times other standards much closer to physiological minimums have been devised to apply in emergency situations where food supplies may be restricted over considerable periods of time.[22] In each instance the standards contain not only average per capita calorie allowances but detailed recommendations as to intake of a variety of vitamins and minerals. The purpose of these comments is not to question or criticize these emergency nutrition standards. Rather, it is to contrast these standards and the policy of setting standards for a variety of vitamins and minerals with the views and policies of our British colleagues based on their extensive experience in Great Britain and Europe during World War II. The nutrition standards adopted in Great Britain for long-term peacetime use differ from the 1948 Recommended Dietary Allowances (U. S. A.) in only minor details. However, their position as to standards for feeding of civilians in time of war differs considerably from current thinking in this country. The British views have been expressed in a recent article by the late Sir Jack Drummond.[9] In essence, their position is that calories are the all-important consideration. Their philosophy can be expressed by the statement: Take care of the calories and the proteins, vitamins and minerals will take care of themselves. In their experience, 2,900 calories (about 3,000 as calories are calculated in this country) per capita per

day in the form of family food supplies is sufficient to enable a population to undertake physically all of the tasks a grave emergency will present. Furthermore, with equitable distribution, this supply of food can be made to cover all nutritional requirements without recourse to artificial supplementation of the diet. This position is predicated on equitable distribution and on the availability of the types of food which formed the basis of their wartime diet, i. e., potatoes, wheat, fresh vegetables and in the case of Great Britain, fairly liberal quantities of milk differentially distributed according to need. Drummond notes that a deficiency of calories is reflected with surprising speed in signs of a very characteristic nature, signs more immediately recognizable than any of those associated with a lack of vitamins or protein. From a practical standpoint, he regards the consequences of energy deficiency as vastly more important than those of any other shortage. It affects morale surprisingly quickly. Discontent, grumbling and irritability are characteristic signs associated with a reduction in calorie intake of about 20%, particularly when it affects those engaged in physical work.

It is possible to devise differential rationing schemes which will enable all groups of the population to get along fairly well for considerable periods on average daily per capita calorie intakes down to about 2,000. Work output may not be optimal and other signs of energy deficiency may be apparent, however. Below this level the task of allotting the available food becomes more and more difficult until a point is reached at about 1,500 calories at which it is impractical to do more than plan for survival unless part of the population is deliberately starved in order to enable the remainder to work.

There is little disagreement between British and American groups on the harmful effects of calorie deficiency and on the approximate levels required to maintain work output and prevent weight loss. Keys [23] has recently summarized in THE JOURNAL the available information on energy requirements of adults. The point of special interest in the views expressed by Drummond is the primary emphasis on calories and the lack of detailed consideration of protein and other nutrient requirements. From the administrative standpoint, this concept would permit a tremendous simplification of wartime food planning.

SUMMARY

This review presents a summary of the physiological and psychological factors involved in disaster feeding. Nutrition standards for various types of disaster feeding have been outlined. The potential importance of intensive nutritional therapy of casualties has been discussed.

A deliberate attempt has been made to emphasize the practical importance of adequate emergency feeding in disasters. Emergency feeding is much more than just a means of providing nourishment to those unable to provide for themselves. It constitutes a powerful tool for calming disturbed and even panic-stricken persons. Its effect on morale is probably more important than its physiological effects especially in the first days of the disaster. These facts are often overlooked in Civil Defense planning in this country.

Although the importance of emergency feeding has been emphasized to the exclusion of other important activities in Civil Defense, the implication is not intended that other activities of Civil Defense are unimportant. All components of Civil Defense are important and all must function together if maximum resistance to attack is to be attained. Indeed, this review has not even touched many important aspects of emergency feeding. Factors of greatest interest to physicians have been selected for emphasis. General sanitation, food and water supply and transport, emergency feeding equipment, training of workers, and measures for the decontamination of food and water are other aspects of emergency feeding which have obvious importance.

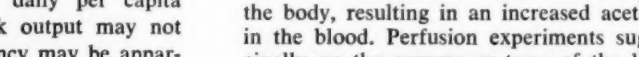
COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

R. T. STORMONT, M.D., *Secretary.*

Disulfiram.—Antabuse (Ayerst, McKenna & Harrison).—$C_{10}H_{20}N_2S_4$.—M.W. 296.54.—Bis(diethylthiocarbamyl)disulfide.—The structural formula of disulfiram may be represented as follows:



Actions and Uses.—Disulfiram, an antioxidant, apparently interferes with the normal metabolic degradation of alcohol in the body, resulting in an increased acetaldehyde concentration in the blood. Perfusion experiments suggest that it acts principally on the enzyme systems of the liver. It does not affect the rate of elimination of alcohol from the body. Regular oral administration of disulfiram, if followed by the ingestion of small amounts of alcohol, causes a highly unpleasant reaction, the severity of which can be correlated with the blood levels of acetaldehyde and ethyl alcohol. It produces no significant effects even after prolonged administration, unless alcohol is introduced into the body. Disulfiram is useful, therefore, for producing a sensitivity to alcoholic beverages as an aid in the treatment of alcoholism. Its use requires the consent and full knowledge of the patient and the application of psychotherapeutic measures designed to rehabilitate the patient. Patients should be advised of the symptoms to be expected if drinking is resumed, and relatives should be instructed concerning the danger of secret administration of the drug. Personality changes have been reported as a consequence of the sudden withdrawal of alcohol, particularly when disulfiram was administered against the wishes of the patient. A complete history, preferably in the presence of a relative, and a thorough physical examination are essential.

The effectiveness of disulfiram as an aid in overcoming the drinking habit depends upon the demonstration of the unpleasant effects produced following ingestion of even a small amount of alcohol, particularly when disulfiram was administered of 15 cc. of 100 proof whisky followed immediately by small amounts of other alcoholic beverages, if such intoxicants might be used by the patient, and demonstrating the reaction produced on others or the patient himself following drug therapy.

Because disulfiram at the dosage now advised is slowly absorbed by the intestinal tract, therapy must be maintained preferably for about three weeks before the drug can be counted on to produce a satisfactory reaction to the ingestion of alcohol. Since it is slowly excreted from the intestinal tract, symptoms will follow the ingestion of alcohol taken as long as a week after administration of a single large dose of the drug, indicating that it has a prolonged effect.

The reaction produced by disulfiram and alcohol is characterized by flushing, palpitations, dyspnea, hyperventilation, acceleration of pulse rate, anoxia, fall in blood pressure, nausea, vomiting, and occasionally collapse. Drowsiness usually follows with complete recovery after sleep. The severity of the reaction varies with each person and with the amounts of disulfiram and alcohol taken. All types of alcoholic beverages will produce a reaction in patients receiving disulfiram when the blood alcohol concentration is increased to as little as 5 to 10 mg. per 100 cc. Fully developed symptoms are observed at a level of 50 mg. per 100 cc.; unconsciousness occurs at levels of 125 to 150 mg. per 100 cc. Heavy drinkers may tolerate larger amounts, but tolerance to alcohol tends to dis-

appear with continued administration of the drug. Tolerance to disulfiram does not develop, nor is it habit forming.

Although disulfiram is of low toxicity when used in the recommended dosage, extreme caution is necessary during its use because severe and alarming reactions to alcohol have been reported in patients on disulfiram. These include cardiovascular complications involving unusual fall in blood pressure, cardiac arrhythmia, electrocardiographic evidence of myocardial ischemia, and even myocardial infarction. Such reactions have resulted usually from excessive trial doses of alcohol or surreptitious drinking during initial stages of treatment; therefore, careful and continuous medical supervision is important.

Some patients on disulfiram therapy complain of mild drowsiness, fatigability, impotence, headache, or peripheral neuritis, but such symptoms tend to subside with continuation of the drug at a reduced dosage. Because of neurologic changes in animals and toxic psychoses observed in human beings receiving large doses, it is essential to limit the daily dose of the drug. Rare instances of skin eruption, which can usually be controlled by concomitant administration of one of the antihistamine drugs, have been reported.

Although there are no known absolute contraindications, the alcohol test is usually omitted when disulfiram is to be given to patients over 50 years of age or employed in the presence of diabetes mellitus, goiter, epilepsy, psychosis, cirrhosis of the liver, or chronic or acute nephritis. The alcohol test must not be given to patients with myocardial failure, coronary disease, or pregnancy. Caution should be exercised when addiction to narcotics is superimposed on alcoholism.

When sedation is required, strict supervision is essential to prevent habituation to barbiturates as a substitute for alcoholism. Disulfiram should not be used in patients recently treated with paraldehyde, and paraldehyde should not be given to patients receiving disulfiram. Disulfiram itself may produce a calming effect conducive to sleep that may lessen the need for sedatives.

Dosage.—Disulfiram is administered orally. The patient should not consume any alcoholic beverage for at least 12 hours before the drug is administered. It is particularly important to refrain from treatment when intoxication is present. The initial dosage should be limited to a maximum of 0.5 gm. daily for the first two or three weeks, and subsequent maintenance dosage should not exceed that amount. The usual maintenance dose is about 0.25 gm., ranging from 0.125 to 0.5 gm. daily. The dosage should be sufficient for the patient to experience flushing of the face after taking 15 cc. of 100 proof whisky or its equivalent (approximately 7.5 gm. of 95% alcohol). Uninterrupted administration of the drug should be continued until the patient is socially recovered and a basis for permanent self-control is established. Since therapy depends on the individual patient, it may need to be continued for a period lasting from several months to years. When indicated, a test dose of alcohol is given after the first two or three weeks of therapy. This should be carefully supervised by the physician, in a hospital if necessary, and a supply of oxygen should be readily available for administration in the event of a severe reaction.

Tests and Standards.—

Physical Properties: Disulfiram is a white to light gray, odorless and almost tasteless powder, m.p. 72-73°. The amounts which dissolve in the following solvents to form 100 ml. of solution are: 3.82 gm. in alcohol, 7.14 gm. in ether, and 0.02 gm. in water.

Identity Tests: Dissolve about 5 mg. of disulfiram in 5 ml. of methanol and add 1 ml. of 0.01% methanolic cupric chloride ($CuCl_2.2H_2O$): A green color develops, changing rapidly from yellow-green to deep green.

Perform a sodium fusion on about 50 mg. of disulfiram. To a 5 ml. portion of the alkaline filtrate add acetic acid until the solution is acid to litmus and then add 3 drops of lead acetate T.S.: a black precipitate forms *(presence of sulfur).*

Purity Tests: Using the residue from the ash determination, dissolve it in 20 ml. of water and add 2 ml. of acetic acid. Dilute to a volume of 25 ml. with water and run a U.S.P. heavy metals test: the amount of heavy metals does not exceed 40 ppm.

Dry about 1 gm. of disulfiram, accurately weighed, in a vacuum oven at 60° for 4 hours: the loss in weight does not exceed 0.5%.

Ash about 1 gm. of disulfiram, accurately weighed: the residue does not exceed 0.5%.

Assay: (Nitrogen) Run a *U.S.P.* semi-micro Kjeldahl determination on about 0.2 gm. of disulfiram, accurately weighed. Each milliliter of 0.1 *N* acid is equivalent to 0.001401 gm. of nitrogen and 0.01483 gm. of disulfiram. The amount of nitrogen is not less than 9.21 nor more than 9.68%, equivalent to not less than 97.5 nor more than 102.5% of disulfiram.

(Sulfur) Place about 15 gm. of sodium peroxide and 1.5 gm. of potassium nitrate in a Parr bomb and mix thoroughly. Add about 0.4 gm. of sucrose and 1 gm. of potassium chlorate, mix, and then add 0.2 gm. of finely powdered disulfiram, accurately weighed. Tighten the cap with a wrench and shake the mixture for 45 sec. Place the bomb in a short length of steel pipe, supported vertically over a Bunsen burner. Put a few drops of water on the top of the bomb cap. Light the burner and place it directly under the bomb. (*Caution!* Wear goggles. View the operation by means of a slanting mirror placed at the top of the apparatus.) Heat the bomb until fusion occurs, as shown by the sudden boiling of the water on the bomb cap (about 45 sec.). Allow the bomb to cool for 1 min., then plunge it into cold water. Rinse the bomb in water, remove the cap, and place the bomb cup in a 400 ml. beaker. Carefully wash off the cover into the beaker. Cautiously add 200 ml. of water, cover the beaker with a watch glass, and allow the fused mass to dissolve completely. Remove the cup from the beaker and rinse carefully into the beaker. Heat the solution and washings cautiously to complete the decomposition of the excess sodium peroxide and to expel the hydrogen peroxide formed. Acidify the solution by slowly adding 35-40 ml. of hydrochloric acid, heat to boiling, and filter the hot solution into a 800 ml. beaker. Wash the filter and add the washings to the filtrate. Dilute the filtrate and washings to about 400 ml. and add 10% barium chloride until no further precipitation occurs. Digest the mixture on a steam bath for 2 hours and collect the barium sulfate on an ashless filter paper. Wash the precipitate with water until the filtrate is free of chloride, dry it, and ignite it to constant weight in an ignited, tared porcelain crucible. Each gram of barium sulfate found is equivalent to 0.1374 gm. of sulfur and 0.3176 gm. of disulfiram. The amount of sulfur is not less than 42.2 nor more than 44.3%, equivalent to not less than 97.5 nor more than 102.5% of disulfiram.

Dosage Forms of Disulfiram

TABLETS. (Disulfiram) The powdered tablet material responds to the identity tests for the active ingredient in the monograph for disulfiram.

Assay: (Disulfiram) Transfer to a 50 ml. volumetric flask about 0.1 gm. of disulfiram (97.5-102.5% pure), accurately weighed, fill to the mark with chloroform, and mix. Transfer to a 100 ml. volumetric flask 5 ml. of this solution, fill to the mark with methanol, and mix. Transfer to 25 ml. volumetric flasks 1, 2, 3, and 4 ml. of this solution, equivalent to 0.1, 0.2, 0.3, and 0.4 mg. of disulfiram, respectively. Fill to the marks with 0.01% methanolic cupric chloride ($CuCl_2.2H_2O$) and mix. Using the reagent as a blank, spectrophotometrically determine the absorbancies in 1 cm. quartz cells at 400 mμ during the following 3-4 min. and record the highest value obtained. Plot the concentrations against the readings obtained to give a standard curve. Weigh 20 tablets and grind them to a fine powder. Transfer to a 50 ml. volumetric flask an amount of powder, accurately weighed, equivalent to about 0.1 gm. of disulfiram. Add about 25 ml. of chloroform, mechanically shake the flask for 10 min., fill to the mark with chloroform, and mix. Transfer to a 100 ml. volumetric flask 5 ml. of the supernatant solution, fill to the mark with methanol, and mix. Transfer to a 25 ml. volumetric flask 4 ml. of this solution and proceed as directed in the preparation of the standard curve starting with, "Fill to the mark with 0.01% methanolic cupric chloride . . ." Read the amount of disulfiram from the standard curve. The amount of disulfiram is not less than 90.0 nor more than 110.0% of the labeled amount.

Ayerst, McKenna & Harrison, Ltd., New York.

Tablets Antabuse: 0.5 gm. U. S. patent 2,567,814.

Carbacrylamine Resins (See THE JOURNAL, Jan. 17, 1953, p. 210).

Eli Lilly & Company, Indianapolis.

Powder Carbo-Resin (Unflavored): 450 gm. A mixture containing about 0.59 gm. of carbacrylic resin, 0.285 gm. of potassium carbacrylic resin, and 0.12 gm. of polyamine-methylene resin in each gram of powder.

CORRECTION

Hexamethonium Salts.—In a Report to the Council, "Uniform Potency for Injectable Solutions of Hexamethonium Salts," in THE JOURNAL, April 11, 1953, page 1289, the following statements were partly in error: "On the basis of comparative molecular weight, hexamethonium chloride provides about one-tenth and one-third more of the active ion than equal amounts of the bitartrate and bromide respectively. The magnitude of these differences is significant only in the comparative dose of the bromide, particularly when that salt is administered parenterally." In the first sentence, "one-tenth" should have read "seven-eighths." In the second sentence, "bromide" should have read "bitartrate."

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EPIDEMIC HEMORRHAGIC FEVER

During the month of June, 1951, there were admitted to the United States medical installations in Korea, according to Col. Joseph McNinch,[1] chief of preventive medicine, Far East Command, several patients with acute febrile disease with symptoms and signs not previously encountered among United Nations personnel in Korea. There was an abrupt onset with malaise, chills, fever, headache, blurred vision, nausea, and vomiting. These symptoms were somewhat later associated with hemorrhagic manifestations, such as petechial rash, marked injection of the conjunctivas, hematuria, and hematemesis. The white blood cell count, normal in the first few days, later manifested a leukemoid reactions with counts from 20,000 to 93,000 per cubic millimeter. In all cases there was severe albuminuria. Jaundice was never present. The case fatality rate during the first peak of the epidemic of this apparently new disease fluctuated between 13 and 18%. Both United States and Japanese observers agreed that from the standpoint of microscopic pathology the disease was the same as that experienced by the Japanese army in Manchuria during 1939 to 1941. The Japanese investigators believed that the disease is carried by a rodent host and that it is probably propagated by an ectoparasite vector.

Ganong and his co-workers [2] state that the earliest symptoms of the disease are headache, which is characteristically retro-orbital, pain in the lumbar area, anorexia, and less commonly nausea and vomiting. The characteristic physical signs consisted of erythema of the face and neck, conjunctival injection and edema, intense pharyngeal injection, and petechia that first appeared on the palate and later in the axillary folds. Albuminuria was a rather typical finding in most cases. There were also found in the urine large oval mononuclear cells and large amounts of a fatty substance. The significance of these two has not been determined. There was polymorphonuclear leukocytosis, with a count ranging between 20,000 and 93,000.

Kessler [3] emphasized in his postmortem studies of 27 fatal cases of epidemic hemorrhagic fever that the most prominent findings were those of vascular changes consisting of edema, congestion, and hemorrhage involving most of the organs, but particularly conspicuous in the anterior pituitary, the kidneys, and the right atrium. Extensive retroperitoneal edema was found in all cases in which autopsy was performed in the earlier stages of the disease.

Hullinghorst and Steer [4] state that among the prominent symptoms in the terminal picture were oliguria, anuria, uremia, one or more episodes of shock, and occasionally severe hemorrhage and pulmonary edema. Shock and renal failure were especially prominent both during the course of the disease and as an immediate cause of death. Shock was an important factor in causing death during the first week of illness. Renal failure was the major cause of death after the first week. Medullary hemorrhage and necrosis were the most prominent findings in the kidney. These authors believe that epidemic hemorrhagic fever as seen in United Nations troops in 1951 in Korea is identical with the disease described by the Japanese in Manchuria and probably identical with the disease described by the Russians in Siberia. The causative agent has not been determined but is probably a Rickettsia organism or a virus. The pathological features observed in autopsies in 61 fatal cases were hemorrhage, particularly in the renal medulla, the right atrium and submucosa of the gastrointestinal tract; a peculiar type of necrosis of the renal medulla, anterior lobe of the pituitary, the adrenal, and occasionally the islands of Langerhans; and a mononuclear cellular infiltration of the myocardium, pancreas, spleen, and liver. Neither the site of entrance nor the site of propagation of the causative agent is recognized. The pathological changes in the fatal cases appear to be produced by a potent circulating toxic agent acting on the capillaries, renal medulla, and certain portions of endocrine glands.

Leedham [5] points to capillary damage as the key to the pathological picture. This would explain the petechiae, the ecchymoses, the varying degrees of widespread hemorrhage, and the pathological changes resembling those of acute glomerular nephritis. The capillary damage could also explain the early transudation of fluid into the tissue spaces. The renal physiology so closely resembling that of acute glomerular nephritis can also be accounted for by glomerular capillary fragility. This plausible explanation, Leedham [5] admits, does not explain all of the phenomena observed in this disease. The absence of retinal hemorrhages, for ex-

1. McNinch, J. H.: Far East Command Conference on Epidemic Hemorrhagic Fever: Introduction, Ann. Int. Med. **38**: 53-60 (Jan.) 1953.

2. Ganong, W. F., and others: The Early Field Diagnosis of Epidemic Hemorrhagic Fever, Ann. Int. Med. **38**: 61-66 (Jan.) 1953.

3. Kessler, W. H.: Gross Anatomic Features Found in 27 Autopsies of Epidemic Hemorrhagic Fever, Ann. Int. Med. **38**: 73-76 (Jan.) 1953.

4. Hullinghorst, R. L., and Steer, A.: Pathology of Epidemic Hemorrhagic Fever, Ann. Int. Med. **38**: 77-101 (Jan.) 1953.

5. Leedham, C. L.: Epidemic Hemorrhagic Fever: A Summarization, Ann. Int. Med. **38**: 106-112 (Jan.) 1953.

ample, is difficult to explain in the presence of widespread capillary fragility. The liver and the spleen are very little affected; there is also no ready explanation for the selectively heavy subendothelial hemorrhages limited sharply to the right atrium and the renal pelvis. It is also not clear why the medulla portion of the kidney exhibits heavy hemorrhage while the cortex shows almost no evidence of hemorrhage. The unusually high leukocyte count found in this disease is not characteristic of viremia.

In a recent contribution in THE JOURNAL, Katz and his co-workers [6] point out that the usual therapeutic measures in the treatment of hemorrhagic fever have been disappointing. Antibiotics, corticotropin, cortisone, convalescent serum, and convalescent whole blood have all failed to have a significant effect. Since most of the deaths due to hemorrhagic fever have occurred during the acute shock phase, certain principles of management, they point out, have resulted in the most successful treatment of this phase. These were prompt and atraumatic evacuation by litter, conservative fluid management based on detailed intake and output records, treatment of shock with Trendelenburg position, elastic bandages on lower extremities, vasoconstrictors, and concentrated human albumin, each used alone and to its maximal effectiveness on the basis of careful determinations of blood pressure. Hemorrhagic manifestations may be minimized by careful handling of the patient, atraumatic evacuation, and sedation. The intensive investigations thus far carried out have shed much light on this new disease, but many problems still remain to be solved.

PROTEIN SYNTHESIS AND CORTISONE

One of the manifold effects of the injection of adrenal cortical extract or of adrenal steroids is the increase in output of nitrogen in the urine of either fasting or fed animals. It appears that this phenomenon is a particular function of those cortical steroid hormones having an oxygen substitution at the C_{11} position. It has been shown [1] that similar injections with animals subjected to hypophysectomy or adrenalectomy augment, in like manner, the basic nitrogen excretion, whereas loss of cortical secretion is followed by a diminution of nitrogen output.[2] It seems plain that the loss of nitrogen in the urine following the administration of cortisone may arise from either accelerated breakdown of body protein or the inhibition of synthesis of tissue proteins from amino acids, which precursors then accumulate and are excreted by the kidney.

In order to determine the mechanism of the observed effect of the steroid cortical hormone on nitrogen metabolism, a study [3] has recently been conducted in which cortisone was administered to intact animals and to animals subjected to adrenalectomy and the partition of urinary nitrogen examined. In addition, the rate of tissue protein synthesis was estimated after the administration of labeled (N^{15}) glycine according to the procedure of Sprinson and Rittenberg.[4] The data on body weight during the period of controlled food intake show that the hormone interfered with protein metabolism, inasmuch as the rats (intact as well as without adrenals) receiving cortisone lost more weight than did the controls without the hormone. The effect of cortisone is shown again by the fact that the intact controls with normal amounts of endogenous cortisone lost more urea nitrogen during the experimental period than did the animals that had undergone adrenalectomy but did not receive injections of cortisone. The proportion of the dose of labeled glycine appearing in the urine was greater in the intact animals or those without adrenals receiving the hormone than in the appropriate control rats. The calculated rate of protein synthesis indicates that, after administration of cortisone, there was an over-all decrease in both intact animals and animals from which adrenals had been removed. On the basis of the foregoing observations, it appears that the loss of nitrogen after administration of cortisone is due to the interference with protein synthesis by the hormone.

A second group of rats was similarly treated except that, at the end of the experimental period, the serum, defatted carcass tissue, liver, the alcohol-ether extract of the carcass, and the urine were analyzed for nitrogen and N^{15}. The data for the total nitrogen, nonprotein nitrogen, and N^{15} of the carcass tissue and extract again support the concept of diminished protein synthesis after the administration of cortisone; however, the livers of the hormone-treated animals were larger and the analytical data indicated that cortisone increases the rate of protein synthesis in this organ, a conclusion supported by an elevated level of serum protein concentration and a relatively greater concentration of N^{15} in the serum of these animals. One suggestion for the different behavior of the hepatic tissue is that the protein precursors accumulated as a result of the depressed protein synthesis in the large mass of extrahepatic tissue stimulate the liver to extra activity to remove these precursors, with the result that its synthetic processes are accentuated. The dominant picture, however, is that of over-all suppression of tissue protein synthesis; this phenomenon would appear to be worthy of special attention at this time when cortisone is being employed in such diverse clinical situations.

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6. Katz, S.; Leedham, C. L., and Kessler, W. H.: Medical Management of Hemorrhagic Fever, J. A. M. A. **150**: 1363-1366 (Dec. 6) 1952.

1. Long, C. N. H.; Katzin, B., and Fry, E. C.: The Adrenal Cortex and Carbohydrate Metabolism, Endocrinology **26**: 309, 1940.

2. Evans, G.: The Adrenal Cortex and Endogenous Carbohydrate Formation, Am. J. Physiol. **114**: 297, 1936.

3. Clark, I.: The Effect of Cortisone upon Protein Synthesis, J. Biol. Chem. **200**: 69, 1953.

4. Sprinson, D. B., and Rittenberg, D.: The Rate of Interaction of the Amino Acids of the Diet with the Tissue Proteins, J. Biol. Chem. **180**: 715, 1949.

ORGANIZATION SECTION

FEDERAL MEDICAL LEGISLATION

Doctor Draft

The long-awaited "Doctor-Draft bill" was introduced April 1 by Senator Saltonstall of Massachusetts and Senator Hunt of Wyoming at the request of the Department of Defense. This extends the expiration of the "Doctor-Draft bill" from July, 1953, to July 1, 1955, continues the upper age limit for induction at 51, and continues the present priorities.

Priorities.—Priorities 1 and 2 include former members of the ASTP and V-12 training program during World War II and those draft-deferred during World War II for educational purposes. Priority 3 are nonveterans and priority 4, veterans with service since Sept. 16, 1940.

Required Length of Service.—The required length of service (in the absence of a declaration by Congress of war or national emergency) is for a maximum of 24 months, except that (1) reservists and nonreservists who have served 12 months or more since June 25, 1950, could not be recalled under the Doctor-Draft act and (2) reserves who have served 12 months or more since Sept. 16, 1940, would be required to serve no more than 17 additional months.

Definition of Prior "Active Duty."—Active duty for purposes of prior service credit is defined as time spent (*a*) on active duty or active duty for training in Army, Navy, Air Force, Marine Corps, Coast Guard, or U. S. Public Health Service, (*b*) on nonmilitary duty prescribed for a conscientious objector, and (*c*) in the military service of a co-belligerent of the U. S. in World War II. Not accepted as active duty would be time spent in ASTP, V-12, or similar training programs, or in "intern training, residency training, or other postgraduate training or in senior student programs prior to receipt of a professional degree."

Termination of Reserve Commissions.—Unless an officer had obligations for reserve service not originating in the Doctor-Draft act, his reserve commission would terminate automatically on completion of his active duty. This provision would be retroactive to Sept. 9, 1950.

Liberalization of Commissioning Procedure.—Aliens otherwise qualified for service would not remain ineligible for commissioning solely because of their alien status or because they have not declared their intention of becoming citizens. The bill attempts to assure that a man's professional qualifications shall determine his grade for commission. This bill, S. 1531, was referred to the Armed Forces Service Committee.

Crediting Internment Time for Purposes of Doctor Draft

Senator Potter (R., Mich.) in S. 1494 and Congressman Budge (R., Idaho) in H. R. 4200 propose to give credit as U. S. military service for the purposes of the doctor draft for time spent in internment for U. S. civilians captured by Germany, Italy, or Japan while such civilians were engaged in national defense activities in World War II. This bill was referred to the Armed Services Committees.

Emergency Maternity and Infant Care

Senator Murray (D., Mont.) in S. 1495 would reestablish an emergency maternity and infant care program similar to that in World War II for the care of wives and infants of enlisted members of the armed forces. The funds would be administered through the Children's Bureau. A state to be eligible would be required to provide (*a*) for the administration of the plan by the state health agency, (*b*) that such agency make reports as required by the Administrator of the Federal Security Agency, and (*c*) for cooperation with medical, nursing, and hospital groups and organizations. The extent of the federal aid would depend upon the financial need of each state and the number of live births to wives of enlisted servicemen. The program would terminate when the President declares an end to the national emergency proclaimed Dec. 16, 1950. This was referred to the Labor and Public Welfare Committee.

Voluntary Coverage Under Social Security for Physicians, Lawyers, Dentists, and Certain Others

Senator Kefauver (D., Tenn.) proposes in S. 1470 to permit physicians, lawyers, dentists, osteopaths, veterinarians, chiropractors, and optometrists to elect coverage in social security on the same basis as for certain other self-employed. Annual contributions would amount to 2¼% (current rate) of the first $3,600 in earnings. This bill was referred to the Finance Committee.

Treaties and Executive Agreements

Congressman Hebert (D., La.) in H. J. Res. 230 proposes to amend the Constitution to invalidate any provision of a treaty that denies or abridges the rights guaranteed by the Constitution. Treaties would become effective as internal law within the United States only after enactment of proper legislation by both branches of Congress. Identical with S. J. Res. 1 (Bricker) and several other previously reported measures. Referred to the Judiciary Committee.

Industrial Safety Act

Congressman Bailey (D., W. Va.) in H. R. 4145 would provide federal funds to assist states in improving safety conditions in industry. The Department of Labor would administer the federal funds and apportion them to the states submitting acceptable programs. The proportion of federal contribution would depend upon population, number of wage-earners, special hazards in industry, number of workers afforded protection, and "the financial needs of the states." An industrial safety advisory committee would assist the Secretary of Labor with this program. This measure was referred to the Education and Labor Committee.

Federal Commission for Physically Handicapped

Congressman Donohue (D., Mass.) in H. R. 4262 proposes to establish an independent agency for the handicapped based in the Department of Labor. The functions of the Office of Vocational Rehabilitation at present in the FSA would be transferred to the new agency. New divisions for the handicapped would be created in the U. S. Civil Service Commission and the U. S. Employment Service. Provision is made for payment through the states for pensions of $60 a month to those whose rehabilitation is unfeasible. This bill is identical with H. R. 2096 (Hagen, R., Minn.), H. R. 2147 (Tollefson, R., Wash.), H. R. 2149 (Van Zandt, R., Pa.), H. R. 2300 (Rhodes, D., Pa.), H. R. 2342 (Wier, D., Minn.), and H. R. 2346 (Withrow, R., Wis.). This bill was referred to the Education and Labor Committee.

STATE MEDICAL LEGISLATION

Illinois

Bill Introduced.—S. 243, proposes to authorize the use in court of the results of **chemical analyses of a defendant's blood, urine, breath, or other bodily substance** providing that the person has expressly consented to the taking of the specimen and providing that the chemical analysis was conducted by a licensed physician or by a person holding a certificate of competency issued by the state department of public health to perform such analysis. If a person refuses to submit to a test that fact may not be referred to in any way against his interest in any civil or criminal proceedings.

Michigan

Bills Introduced.—H. 456, proposes the creation of a **department of professional licensing.** This department would conduct the administrative details necessary in a licensure program. Within the department would be a three-member council for each profession licensed by the department,

The summary of federal legislation was prepared by the Washington Office of the American Medical Association and the summary of state legislation by the Bureau of Legal Medicine and Legislation.

and this council would handle the preparation, conduct, and grading of all examinations and consult with and advise and make recommendations on policy to the director of the department. H. 457, proposes the enactment of an **office of health affairs act.** It proposes the creation of a state office of health affairs which shall consist of a bureau of hospital survey and construction, a bureau of alcoholism, and such other bureaus as may be necessary in carrying out the functions of the department.

Minnesota

Bills Introduced.—H. 1702, proposes that **tissue removed in surgical operations,** except in operations on tonsils, hemorrhoids, lipomas, and wens and tissue irreparably destroyed by bodily injury, shall be forwarded to pathological laboratories approved by the department of health, the mode of preparation, transportation, and amount of tissue to be prescribed by the department of health. The pathological report shall forthwith be filed with the department of health and a copy forthwith transmitted to the hospital at which the operation was performed and copies of the report on file with the department of health shall be available for inspection to all persons licensed in the healing arts. H. 1742, proposes the creation of a **commission to investigate and study the county coroner system** in the state. S. C. R. 27, proposes the creation of an interim **commission to study the office of coroner and other related medical examiner systems** and to have authority to and shall study the laws relating to said office of coroner and other similar offices provided for by law in other states. According to this proposal the special committee should also consider the various laws and systems used in other states relating to the office of coroner or medical examiner systems and make a determination and recommendation of the need for a revision of the laws of the state of Minnesota relating to said office of coroner and the development of a new or improved system of a modern, scientific determination of the cause of death. S. 1551, proposes a codification and revision of existing laws relating to **workmen's compensation.**

Missouri

Bills Introduced.—H. 402, proposes the establishment of a state children's hospital to provide the proper custody, care, and treatment of eligible children not over the age of 6 who are afflicted with **cerebral palsy.** S. 392, to amend the law relating to chiropractic, proposes **to define the practice of chiropractic** to be the art and science of palpating the spinal column, diagnosing, and the adjusting of the movable segments of the spinal column and tissues adjacent thereto by hand. It shall include the use of such supplementary measures as light, heat, electricity, cold, air, water, dietetics, rest, and exercise. It shall not include the use of operative surgery, obstetrics, osteopathy, nor the administration or prescribing of any drug or medicine.

New York

Bill Enacted.—A. 907, has become ch. 124 of the laws of 1953. It amends the law relating to **confidential communications** by providing that a registered professional or a licensed practical nurse shall not be allowed to disclose any information acquired in attending a patient in a professional capacity and which was necessary to enable the nurse to act in that capacity, except under certain conditions of waiver.

North Carolina

Bills Introduced.—S. 86, proposes, among other things, that it shall be the duty of every attending or consulting **physician to report** to the state board of health promptly the name of any person under treatment when it appears that such person is an **habitual user of any narcotic drug.** S. 343, proposes to make it unlawful for any owner exhibiting **three dimensional motion pictures** or any other amusement requiring the use of polaroid glasses by the public in viewing such entertainment to reissue such glasses or devices to the public after they have been worn or used by the public or to cause or permit such reissuance or reuse.

Ohio

Bills Introduced.—H. 359, proposes to authorize county commissioners to establish and maintain **mental health clinics** and to employ physicians and public health nurses in the maintenance and operation of such clinics. H. 552, to amend the **workmen's compensation act,** proposes to authorize a claimant or employer not satisfied with the commission's order to file an application for review of medical questions involved. Upon the filing of this application the matter shall be referred to three **physicians skilled in respect of the medical questions involved** in the claim, and these three physicians shall constitute a medical board of review to hear and pass upon the medical questions involved in the claim. The claimant and the employer may be heard before this board, and a finding of the majority of the board shall be treated as though it were the finding of the commission. S. 155, proposes the creation of a **state department of mental hygiene and correction.**

Oklahoma

Bills Introduced.—H. 1029, proposes that all prescriptions issued for any kinds of narcotics or other drugs shall be issued on **prescription blanks which have no form of advertising,** names, or addresses of persons who dispense said narcotics or drugs and no such advertising shall be displayed in the office of the persons licensed to issue prescriptions. H. 1030, proposes that the **practice of naturopathy,** commonly known as a drugless physical culture to cure disease, be prohibited and any person found guilty of practicing naturopathy shall be guilty of a felony. H. 1031, to amend the law relating to **penalty for narcotic violations,** proposes that on a second or subsequent offense the imposition or execution of sentence shall not be suspended and probation shall not be granted until the minimum imprisonment shall have been served. S. 234, proposes to authorize the state board of health to establish a department of registration for the **registration of professional sanitarians.**

THE PRESIDENT'S MASSEUR

Recently a columnist whose column is syndicated for many newspapers wrote that President Eisenhower while on his campaign tour had with him a personal physician and a chiropractor who gave him a daily checkup. This columnist has previously written favorably on behalf of chiropractors and has in effect claimed they were entitled to a higher professional standing than they are now generally accorded. The columnist is not medically trained, but he does not hesitate from time to time to offer comment on medical items that normally would seem to be outside of his bailiwick. So far as the comment on President Eisenhower's campaign tour is concerned, however, the following exchange of correspondence between Dr. Morris Weintrob and Mr. Sherman Adams should interest physicians.

January 8, 1953

Governor Sherman Adams
Assistant to General Eisenhower
The Commodore Hotel
Lexington Ave. & 42nd St.
New York, N. Y.

Dear Governor Adams:

On page 1 of vol. 19 #11 of "Better Health," a publication of the Science Sidelights Co., Brooklyn 17, N. Y., there appears a featured article stating that a chiropractor helps "Ike" keep health on way to White House. This article states that General Eisenhower "has had a personal physician and a chiropractor along . . . with him during his campaign." It is alleged that the chiropractor gave General Eisenhower a daily check-up.

I would appreciate it very much if you would advise me as to whether or not this information is correct.

Very truly yours,
MORRIS WEINTROB, M.D., Chairman
Subcommittee on Cultists
Legislative Committee
Medical Society of the County of Kings
and Academy of Medicine of Brooklyn
1313 Bedford Avenue
Brooklyn 16, New York.

January 12, 1953

Dr. Morris Weintrob
Medical Society of the County of Kings
1313 Bedford Avenue
Brooklyn 16, N. Y.

Dear Dr. Weintrob:

Your letter of January 8th has just reached me inquiring whether or not President-Elect Eisenhower had a chiropractor who gave him daily check-ups during the campaign.

There has been considerable confusion on this point, since General Eisenhower has a masseur who gives him daily treatments. I do not believe, however, that he is a chiropractor.

Sincerely,
SHERMAN ADAMS
Office of Dwight D. Eisenhower
Commodore Hotel
New York, New York.

The following comment was sent by Major. Gen. Howard McC. Snyder, U. S. Army, President's Eisenhower's personal physician, on Feb. 20, 1953, from the White House to Dr. Walter V. Moore of Brooklyn.

"As a matter of fact, I was interrogated by many officers of the American Medical Association, including the secretary of the association in New York City, with reference to the subject matter of the letter to Adams. I assured everyone that the man we had on board was a simple masseur, uneducated and with no desire to pose as a chiropractor. He was a very personable fellow, exceedingly loyal and willing, and a very good masseur. If you care to publish this statement anywhere, you can quote me."

MEDICAL NEWS

ARKANSAS

State Medical Meeting.—The Arkansas Medical Society will hold its annual session April 20-22 in Little Rock under the presidency of Dr. Sherod A. Drennen, Stuttgart. Symposiums on internal medicine and on obstetrics and gynecology will be held Monday afternoon, and on Tuesday afternoon there will be symposiums in pediatrics, surgery, and eye, ear, nose, and throat. Wednesday morning will be devoted to a "What's New" symposium. A buffet dinner and dance will be held Tuesday at 7:15 p. m. U. S. Senator John L. McClellan will be the speaker. Out-of-state speakers include Dr. George E. Burch, New Orleans, Dr. Samuel F. Haines, Rochester, Minn., Dr. John B. Youmans, Nashville, Tenn., Dr. Emil Novak, Baltimore, and Dr. Allan C. Barnes, Columbus, Ohio.

ILLINOIS

Mental Health Program.—At a dinner meeting, April 21, in the Leland Hotel, Springfield, Dr. Otto L. Bettag, director, Illinois Department of Public Welfare, will discuss the mental health program of the state of Illinois before the annual Mental Health Conference sponsored by the Illinois Society for Mental Health and affiliated mental health societies in Peoria, Rockford, Rock Island, and Springfield. The conference will include a presentation by the New York cast of "My Name Is Legion," the drama of the mental health movement developed by the National Association for Mental Health.

Chicago

Sloan Memorial Research Grant.—Friends of the late Dr. Howard Sloan have instituted a research grant in his memory to be perpetuated to the extent of $500 per year for the benefit of the department of physiology, Chicago Medical School.

Course in Heart Disease.—The Cook County Graduate School of Medicine, 707 S. Wood St., announces a two week intensive course on "Diagnosis and Treatment of Congenital and of Rheumatic Heart Disease in Infants and Children," to be presented by Drs. Benjamin M. Gasul and Egbert H. Fell and associates, May 18-30.

D. J. Davis Lecture.—The 10th D. J. Davis Lecture on Medical History at the University of Illinois College of Medicine, Chicago, will be given May 6 by Richard H. Shryock, Ph.D., director, Institute of the History of Medicine, Johns Hopkins University, Baltimore, on "Changing Concepts in American Medicine Over Three Centuries." The lectureship was established in 1943 by the associates and friends of Dr. David J. Davis on his retirement as dean of the college of medicine.

KENTUCKY

General Practitioners Meeting.—The annual meeting of the Kentucky Chapter of the American Academy of General Practice will be in Louisville April 22-23. The theme of the meeting will be "Recent Advances in Medicine as They Will Apply to General Practice." Speakers include Drs. A. Neal Owens, New Orleans, Albert Weinstein, Nashville, Tenn., Richard E. Goldsmith, Cincinnati, Claude S. Wright and Thomas E. Shaffer, Columbus, Ohio. Senior students at the University of Louisville School of Medicine and interns and residents interested in general practice have been invited with their wives as guests of the Kentucky and Jefferson County chapters at the dinner meeting April 22, at which Dr. Joe M. Bush, Mount Sterling, will speak on "The Meaning of the Academy of General Practice." The E. M. Howard General Practice award will be presented at the dinner.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education and public health. Programs should be received at least three weeks before the date of meeting.

MASSACHUSETTS

Edward K. Dunham Lectureship.—The Faculty of Medicine of Harvard University, Boston, announces that three lectures will be given under the Edward K. Dunham Lectureship for the Promotion of the Medical Sciences on "Natural Acclimatization to High Altitudes" by Dr. Alberto Hurtado, professor of pathological physiology, Faculty of Medicine, and research director, Institute of Andean Biology, Lima, Peru. These studies on native residents of Morococha, Peru, at an altitude of 14,900 ft., will be presented April 21 ("Man at Rest"), April 23 ("Man During Physical Activity"), and April 28 ("General Physiological and Clinical Considerations") at 5 p. m. in the medical school amphitheater, building D. The lectureship, founded in memory of Dr. Edward K. Dunham, aims to bind closer "the bonds of fellowship and understanding between students and investigators in this and foreign countries" and specifies that lecturers be chosen from "eminent investigators and teachers in one of the branches of the Medical Sciences, or of the basic sciences which contribute towards the advance of Medical Science in the broadest sense."

MONTANA

Public Health Meeting.—The Montana Public Health Association will meet in the junior high school building in Lewistown, April 24-25. The guest speaker will be Dr. Franklin S. Crockett, Lafayette, Ind., chairman of the Council on Rural Health of the American Medical Association, who will also address the banquet on Friday.

NEW HAMPSHIRE

Psychiatric Meeting.—The annual meeting of the New England Society of Psychiatry will be held at the New Hampshire State Hospital, Concord, April 22. The host, Dr. John L. Smalldon, will conduct a tour of the hospital at 11:30 a. m. Luncheon, for which a nominal charge of $1 will be made, will be served after the business meeting. At 2 p. m. Dr. Paul H. Hoch, New York State Psychiatric Institute, New York, will speak on "Pseudoneurotic Schizophrenia."

NEW JERSEY

Institute in Psychiatry and Neurology.—The annual Institute in Psychiatry and Neurology, sponsored by the VA Hospital, Lyons, the New Jersey Neuropsychiatric Association, and the New Jersey District Branch of the American Psychiatric Association, will be held April 22-23 at the VA Hospital, Lyons. The following presentations will be made:

Dynamics of the Cure in Psychiatry, Iago Galdston, New York.
Recent Research in Schizophrenia, William Malamud, Boston.
Simultaneous Tactile Tests in Normal and Abnormal Subjects, Morris B. Bender, New York.

At the dinner on Wednesday Dr. Gregory Zilboorg, New York, will speak on "The Humanitarian and the Therapeutic in Psychiatry." At the scientific session on Thursday the following papers will be read:

Relation of Endocrine Glands to Mental Disturbances, Francis J. Braceland, Hartford, Conn.
Modern Methods of Treatment in Psychiatry, Kenneth E. Appel, Philadelphia.
Modern Approach to Diagnosis and Treatment of Brain Tumors, Leo M. Davidoff, New York.

Military and full-time VA personnel are exempt from the registration fee of $1. Additional information may be obtained from Dr. Crawford N. Baganz, VA Hospital, Lyons.

Amputee Conference.—The annual amputee conference will be held at the Kessler Institute for Rehabilitation, Pleasant Valley Way, West Orange, April 24-25. The speakers on Friday will be Mrs. Leona S. Bruckner, mother of an amputee child ("A Parent Speaks"); Dr. Douglas P. Murphy, University of Pennsylvania School of Medicine, Philadelphia ("Statistical Aspects

of Congenital Malformations"); and Dr. Henry H. Kessler, medical director of the institute ("Management of Congenital Amputees"). On Saturday the morning program will be on lower extremity congenital amputations, with panel discussions on surgery, prostheses, and training. The afternoon program, which will present panel discussions on the same subjects in upper extremity amputations, will be introduced by Dr. Lewis H. Loeser, Newark, who will discuss psychological preparation of these patients.

NEW YORK

Society News.—Prof. John McMichael, University of London Post-Graduate Medical School, will address the Medical Society of the County of Kings on April 21 on "Medical Management of Hypertension."——At the annual meeting of the Finger Lakes Neuropsychiatric Society the following physicians were elected for the coming year: president, Benjamin Pollack, Rochester; vice-president, Edwin M. Levy, Canandaigua; and secretary-treasurer, Murray Bergman, Newark.

Tuberculosis Clinical Session.—The Tuberculosis Sanatorium Conference of Metropolitan New York will hold its 57th clinical session April 22, 8:15 p. m., in the amphitheatre of Cornell University Medical College, 1300 York Ave. (at 69th Street), New York. Dr. David Ulmar, New York, will moderate a panel discussion on "Antimicrobial Drugs in the Treatment of the Unhospitalized Tuberculosis Case." Collaborators will be Drs. Benjamin P. Potter, Jersey City, N. J., Harry H. Epstein, Jamaica, Arthur B. Robins, Arthur H. Aufses, H. McLeod Riggins, and Herbert R. Edwards, New York.

Course in Geriatrics.—The University of Buffalo School of Medicine announces a postgraduate course in geriatrics, April 22-23, under the sponsorship of the Western New York Geriatrics Society. Wednesday morning will be devoted to case presentations (arthritis) at Buffalo General Hospital, followed by a panel discussion on "Endocrine Factors in Geriatric Disease." The afternoon session in the Edward J. Meyer Memorial Hospital will consider social and psychological problems, and the Thursday meetings in the same hospital will include discussions on geriatric surgery, nutrition, cerebral vascular accidents, and rehabilitation. The visiting faculty consists of Dr. Norman H. Jolliffe, Dr. Thomas H. McGavack, and Mr. Ollie A. Randall, all of New York. Applications should be sent to Dr. Milton Terris, University of Buffalo School of Medicine, 24 High St., Buffalo 3, together with fee, $25.

New York City

Bancroft Lecture.—The fifth Frederic W. Bancroft Lecture in Surgery, sponsored by the Alumni Association of Beth David Hospital, will be delivered at the hospital on the evening of April 22 by Dr. Arthur P. Stout, pathologist, who will speak on "Relationship of Benign Breast Lesions to Carcinoma."

Ophtho-Otolaryngological Alumni Meeting.—The Alumni Association of the New York Eye and Ear Infirmary will hold its annual scientific program April 20-24, the sessions on ophthalmology being held Monday and the otolaryngological sessions Thursday and Friday at the New York Academy of Medicine, room 440. Morning sessions will commence at 9:30, and afternoon sessions at 2:00. Wednesday will be left open for clinical and surgical demonstrations at the New York Eye and Ear Infirmary. For information, write Dr. Hunter H. Romaine, Secretary-Treasurer, 218 Second Ave, New York 3.

Conference on Multiple Sclerosis.—The New York Academy of Sciences and the National Multiple Selerosis Society are holding a conference on the status of multiple sclerosis, April 17-18, at the Barbizon-Plaza Hotel, 101 W. 58th St. at Sixth Avenue. The morning session will be devoted to biological and pathological methods, with Dr. Harry M. Zimmerman, Montefiore Hospital for Chronic Diseases, New York, as chairman. Francis O. Schmitt, Ph.D., Massachusetts Institute of Technology, Cambridge, will serve as chairman for the afternoon session on biochemical methods. All Saturday sessions will be devoted to consideration of clinical methods, with Dr. Hans H. Reese, University of Wisconsin Medical School, Madison, in the chair. Attendance is limited to those invited to participate in the conferences and to members of the National Multiple Sclerosis Society and of the New York Academy of Sciences.

OHIO

State Medical Meeting.—The Ohio State Medical Association will hold its annual meeting in Cincinnati, April 21-23 under the presidency of Dr. Harve M. Clodfelter, Columbus. The sessions will open with medical motion pictures Tuesday, 8:30-9:15 a. m. in the Pavilion Caprice, Netherland Plaza Hotel, where all general sessions will be held. Out-of-state speakers will present the following papers:

Anesthetic Management of Patients with Heart Disease, Robert D. Dripps, Philadelphia.
Treatment of Renal Tuberculosis with Isonicotinic Acid Hydrazid, Streptomycin and Pas, John K. Lattimer, New York.
Reevaluation of Endocrine Therapy in Obstetrics and Gynecology, Ralph A. Reis, Chicago.
What to Do About Strabismus, Frank D. Costenbader, Washington, D. C.
Bronchoscopy in Relation to Thoracic Surgery, Chevalier L. Jackson, Philadelphia.
Prophylaxis of Accidental Trauma, George M. Wheatley, New York.
Radiation Hazards in Diagnostic Roentgenology, Richard H. Chamberlain, Philadelphia.
The Problem Drinker—A Medical Responsibility, Andrew S. Tomb, Victoria, Texas.
Medical Management of Peptic Ulcer, Joseph B. Kirsner, Chicago.
Surgical Management of Peptic Ulcer, Lester R. Dragstedt, Chicago.
Treatment of Coronary Heart Disease, Charles K. Friedberg, New York.
Surgical Therapy in Portal Hypertension with Particular Reference to Selection of Cases, Louis M. Rousselot, New York.

On Tuesday at 2 p. m. there will be a panel on analgesia and anesthesia in obstetrics, and at 3 p. m. a round-table discussion of sex hormone therapy in gynecology. The Cincinnati Obstetrical Society will sponsor a cocktail and dinner party at the Netherland Plaza Hotel after this meeting (reservations and check for $8 should be sent to Dr. Stanley T. Garber, 104 William Howard Taft Road, Cincinnati 19). The annual banquet will be held Wednesday at 7:30 p. m. in the Pavilion Caprice. Tickets ($6.50) may be ordered from the Columbus office of the association, 79 E. State St., Columbus 15. Other organizations that will meet during the annual session include the Woman's Auxiliary (Hotel Sheraton-Gibson); Ohio Chapter of the American College of Chest Physicians (Hotel Sheraton-Gibson), which will be addressed by Dr. J. Park Biehl, Cincinnati, on "Experiences in the Management of Tuberculous Meningitis"; and the alumni association of Jefferson Medical College, which will hold a dinner get-together at Town and Country, 1622 Dixie Highway, Covington, Ky., April 21. The Ohio State Heart Association will meet April 23, 2 to 4:30 p. m. at the Hotel Gibson. Although this program has been keyed for the general practitioner, all physicians are welcome to attend. There will be no charge or registration fees. On the day preceding the annual state meeting, there will be a conference of all county society officials and committeemen at the Netherland Plaza Hotel. C. Joseph Stetler, LL.M., Secretary, A. M. A. Council on National Emergency Medical Service, Chicago, will talk on "Doctors and the Military Situation."

VIRGINIA

Meeting of Radiologists.—The Virginia Radiological Society will hold its midyear meeting April 24-25 at the Hotel Roanoke in Roanoke. The meeting will begin with a film interpretation session Friday at 8 p. m. On Saturday Dr. Ernest H. Wood, professor of radiology, University of North Carolina School of Medicine, Chapel Hill, will address the luncheon meeting. There will be a dinner Saturday evening.

WASHINGTON

Society News.—The Washington State Medical Association, 338 White-Henry-Stuart Bldg., Seattle, invites submission of titles of medical and surgical papers, together with a 100 word abstract, for possible presentation at the annual convention, Sept. 12-16. Deadline will be May 1.

WISCONSIN

Narcotic Violation.—Dr. Arnt A. Solberg, Coon Valley, was convicted in the U. S. District Court at Wausau of a violation of the federal narcotic law. On Feb. 9 he was sentenced to a term of four months.

Carey Memorial Lecture.—The annual Eben Carey Memorial Lecture, sponsored by Phi Delta Epsilon fraternity, Alpha Lambda chapter, will be given at the Marquette University School of Medicine, Milwaukee, April 22, 4 p. m. Dr. Rachmiel Levine, chairman of the department of medicine and director of education at Michael Reese Hospital, Chicago, will speak on "Present Concept of the Nature of Insulin Reaction." Attendance is open to students and physicians of the community.

GENERAL

Alumni Day.—The annual Alumni Day of the State University College of Medicine at New York City, Brooklyn, April 25, will include a scientific session at the Polhemus Clinic, followed by the annual business meeting. The annual dinner will be at the Hotel Granada, Ashland Place and Lafayette Avenue, Brooklyn.

Health Education Conference.—The Eastern States Health Education Conference of the New York Academy of Medicine, April 23-24, will include four sessions and a Thursday dinner meeting. The subject of the conference will be "Sociology of Health Education." Participation in the conference is limited. Information may be obtained from Dr. Iago Galdston, New York Academy of Medicine, 2 E. 103rd St., New York 29.

Pathologists Meet in Tacoma.—The Pacific Northwest Society of Pathologists will combine its meeting in Tacoma, April 24-25, with that of the Northwest Regional Meeting of the College of American Pathologists. Dr. William S. Hoffman of the Hektoen Institute for Medical Research, Cook County Hospital, Chicago, will present three papers: "Fundamental Features of Disturbances of Potassium Metabolism," "Chemical Findings in Uremia and Their Implication in Management," and "Pathophysiology of Lower Nephron Nephrosis."

Sectional Meeting of American College of Surgeons.—The American College of Surgeons will hold a sectional meeting in Calgary, Alberta, Canada, April 23-24. Thursday morning there will be a symposium on trauma, and Thursday afternoon a symposium on cancer as well as panel discussions on "Surgical Lesions of the Colon, Anus, and Rectum" and "Pre- and Postoperative Care." The Honorable C. C. McLaurin, chief justice, Trial Division of the Supreme Court, Province of Alberta, will deliver the main address at the dinner meeting Thursday evening. The Friday afternoon program will include a panel discussion on "Biliary Tract Surgery" and a symposium on gynecology. Medical motion pictures will be shown both days.

Examinations for Occupational Therapists.—The State of New York Department of Civil Service will hold an examination June 27 to fill 80 occupational therapy positions. The examination is open to all qualified citizens of the United States. Vacancies exist in schools, hospitals, and other state institutions. Salary ranges from $3,251 to $4,052 in five annual increases; for those in tuberculosis service, the range is from $3,571 to $4,372. Candidates must meet, by Aug. 31, either one of the following requirements: (1) graduation from an approved school of occupational therapy or (2) college graduation and completion of at least 10 months of specialized training in an approved school of occupational therapy. Applications will be accepted from April 20 to May 22. Information may be obtained from the State of New York Department of Civil Service, State Office Building, Albany 1, N. Y.

Medical Progress Meeting in Richmond, Va.—When the World Medical Association meets at Richmond, Va., April 23-25 (*J. A. M. A.* **150:**1711 [Dec. 27] 1952), panel discussions will be presented by specialists and general practitioners from all parts of the country. These physicians are each contributing a chapter to a commemorative volume on "Seventy-Five Years of Medical Progress," which will be issued by the World Medical Association. According to Dr. Louis H. Bauer, Hempstead, N. Y., President of the American Medical Association, and secretary-general of the World Medical Association, it "will form a valuable record of every field of medical practice during a most important period of human history, when major gains have been made in the conquest of disease and the lengthening of life." Costs of publication are included in a grant by A. H. Robins Company, Inc., Richmond pharmaceutical house, which covers the cost of holding the conference. Dr. Bauer will serve as moderator at a dinner meeting and summarize the conclusions of the day's panel discussions.

Memorial Meeting in Knoxville.—The Southeastern Section, International College of Surgeons, will hold the Herbert Acuff Memorial Meeting April 24-25 at the Andrew Johnson Hotel, Knoxville, Tenn. Dr. Benjamin T. Beasley, Atlanta, will serve as moderator for a panel discussion Friday, 2-4 p. m., on "Management of Gastrointestinal Hemorrhage," with Drs. Donald T. Chamberlin, Acuff Clinic, Knoxville, Arnold S. Jackson, Jackson Clinic, Madison, Wis., David P. Boyd, Lahey Clinic, Boston, and Daugh W. Smith, Nashville, Tenn., as collaborators. Dr. Acuff will be memorialized by Drs. H. Dewey Peters, Knoxville, and Edward L. Compere, Chicago. The banquet Wednesday evening at the Cherokee Country Club will be addresssed by Dr. Max Thorek, Chicago, who will discuss "The Surgeons' International Hall of Fame" and Dr. Jackson, whose topic will be "Present Concepts of Thyroid Surgery." A symposium on "The Current Use of Radioactive Isotopes" Saturday, 10 a. m. to 12 noon, will be moderated by Dr. Marshall H. Brucer and associates, Oak Ridge (Tenn.) Institute of Nuclear Studies, Medical Division. Scheduled for Saturday afternoon are golf, a trip to Oak Ridge, a trip to Norris Dam, and other activities.

Pediatricians Meet in Boston.—An area meeting of the American Academy of Pediatrics will be held at the Hotel Statler, Boston, April 20-22. Topics for discussion include:

Antibiotics and Chemotherapy in Pediatric Practice.
ACTH and Cortisone in Pediatrics.
Orthopedics and the Pediatrician.
Parenteral Fluid Therapy in Pediatric Practice.
Recent Knowledge of Poliomyelitis.

On Wednesday clinical sessions will be held in the Main Amphitheatre of the Boston Floating Hospital, the Jimmie Fund Amphitheatre of Children's Medical Center, and the "White 3A" Amphitheatre at Massachusetts General Hospital. The banquet will be held at 8 p. m. in the Grand Ballroom. Speaker of the evening will be Dr. Benjamin M. Spock, professor of child development, University of Pittsburgh School of Medicine, who will talk on "The Pediatrician's Family." The members' registration fee of $6.50 includes one banquet ticket; additional banquet tickets may be purchased at $6.50 each. Registration fee for nonmembers out of school more than five years, $25; less than five years, and for those in the Armed Forces and for applicants of the American Board of Pediatrics, $6.50; residents and interns if properly identified, no fee.

Radium Society Meeting.—The annual meeting of the American Radium Society will be held April 20-22 at the Park Plaza and Chase hotels, St. Louis, under the presidency of Dr. Howard B. Hunt, Omaha. Monday, 10:45 a. m., Dr. Frederic E. Mohs, Madison, Wis., will speak by invitation on "Chemosurgery in Cancer Recurrent or Persistent After Irradiation." The Janeway Lecture is scheduled for 12 noon in the Tiara Room, Park Plaza Hotel. Cocktails at 7 p. m. at the Starlite Roof, Chase Hotel, will precede the banquet in the Zodiac Room, which will be followed by dancing at the Chase Club. About 20 formal papers will be presented during the first two days of the session. One-half day will be devoted to clinics at the Washington University School of Medicine, which will include introduction of radiogold into the prostate and into the parametria, demonstration of fixed radium applicators, and the direct measurement of pelvic irradiation. The tumor clinic will provide cases to be discussed by a panel, which will include radiologists, surgeons, and pathologists. The sessions will conclude with a barbecue luncheon sponsored by the St. Louis Radiological Society at the Lazy M. D. Corral at the residence of Dr. Edwin C. Ernst.

Industrial Health Conference.—Constituent groups of this conference, which will meet at the Hotel Statler, Los Angeles, April 18-25, are the Industrial Medical Association, American Conference of Government Industrial Hygienists, American Industrial Hygiene Association, American Association of Industrial Dentists, American Association of Industrial Nurses, Inc., and U. S. Navy 5th Annual Industrial Health Conference. On Tuesday there will be clinics at the Los Angeles County General Hospital. Dr. John L. Norris, Rochester, N. Y., will serve as moderator for a panel discussion on "Human Relations Problems in Industrial Medicine." On Wednesday morning a joint session of the Industrial Medical Association and American Industrial Hygiene Association will have a symposium on noise, with Mr. A. M. Noyes and Dr. Rutherford T. Johnstone, Los Angeles, serving as co-chairmen. A panel on geriatrics and preretirement counseling will be presented Wednesday afternoon at the joint session of the Industrial Medical Association, American Association of Industrial Dentists, and American Association of Industrial Nurses. The annual banquet will be held Wednesday in the Cocoanut Grove. Thursday morning Dr. James H. Sterner, Rochester, N. Y., will moderate a symposium on pneumoconioses.

PHILIPPINE ISLANDS

Medical Association Jubilee.—To mark its Golden Jubilee, the Philippine Medical Association will convene in Manila April 19-26 under the presidency of Dr. Juan S. Salcedo Jr. The meeting will open at 8 a. m. Sunday with a mass for the Philippine Medical Association at the Philippines International Fair Catholic Pavilion. At 9 a. m. after a floral offering at the Rizal Monument, the Jubilee Motorcade will start at the Luneta and end at the University of Santo Tomas College of Medicine Building. At 5:30 p. m. the college and the Santo Tomas University Hospital will give a welcome tea on the campus. Beginning on Tuesday, four plenary sessions will be held at 9 a. m. on succeeding days in the Anatomy Laboratory, Medicine Building, U. S. T.: (1) gerontology; (2) infant mortality; (3) cancer; and (4) general. On Tuesday at 7:30 p. m. in the same laboratory there will be a special session with films on atomic weapons and their effects, courtesy of the Aero Medical Society. A reception and ball will be given by the Manila Medical Society at 8:30 p. m. Monday, and scientific films will be shown by the society at 8 p. m. Friday. At 8:30 p. m. Saturday the Philippine Medical Association will hold a reception and ball at the Manila Hotel. Col. Charles Leedham, U. S. Army Medical Corps, has been designated by the American Medical Association as its representative to the Golden Jubilee celebrations.

FOREIGN

DDT Factory in India.—According to an agreement signed by the Government of India, the United Nations International Children's Emergency Fund (UNICEF), and WHO, a chlorophenothane (DDT) factory is to be constructed in Delhi, which by March, 1954, will produce annually 700 tons of insecticides. The plant will serve also as a training center in modern methods of insecticide production for technicians from other countries. The Indian government will provide the land, buildings, transport within the country, water, and electricity, and will pay for installation of equipment, services of local personnel, and general expenses. UNICEF will procure the essential equipment for the production of DDT and for a control laboratory. WHO will furnish the services of four international experts who will advise on the construction and initial operation of the plant.

CORRECTION

Psychiatrist-in-Chief.—Dr. Theodore Lidz, professor of psychiatry at Yale University School of Medicine, New Haven, Conn., has become psychiatrist-in-chief of the Grace-New Haven Community Hospital. Dr. Stephen Fleck, presently at the University of Washington School of Medicine, Seattle, will become psychiatrist in charge of the Yale Psychiatric Clinic July 1. In THE JOURNAL (March 7, page 830) the title of Dr. Lidz was incorrectly given.

EXAMINATIONS AND LICENSURE

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 23-25. Sec., Dr. D. G. Gill, 537 Dexter Ave., Montgomery.

ARIZONA:* *Examination.* Phoenix, April 21-23. Sec., Dr. J. H. Patterson, 316 W. McDowell Road, Phoenix.

ARKANSAS:* *Regular. Examination.* Little Rock, June 18-19. Sec., Dr. Joe Verser, Harrisburg. *Homeopathic. Examination.* Little Rock, April 6. Sec., Dr. Carl S. Bungart, 105 North 14th St., Ft. Smith. *Eclectic.* Little Rock, June 4-5. Sec., Dr. Frank C. Smith, 2301 Broadway, Little Rock.

CALIFORNIA: San Francisco, June 22-25. Asst. Sec., Mr. Wallace D. Thompson, 1020 N Street, Sacramento 14.

DELAWARE: Dover, July 14-16. Sec., Dr. Joseph S. McDaniel, 229 South State St., Dover.

DISTRICT OF COLUMBIA:* *Examination.* Washington, May 11-12. Commissioner of Licensure, Dr. Daniel L. Seckinger, 4130 East Municipal Bldg., Washington.

FLORIDA:* Jacksonville, June 28-30. Sec., Dr. Homer Pearson, 701 Dupont Bldg., Miami.

GEORGIA: *Examination.* Atlanta and Augusta, June 9-10. *Reciprocity.* Atlanta, June. Sec., Mr. R. C. Coleman, 111 State Capitol, Atlanta.

GUAM: The Commission on Licensure will meet whenever a candidate appears or submits his credentials. Ex. Sec., Dr. Austin W. Matthis, Agana.

HAWAII: *Examination.* Honolulu, July 13-15. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

IDAHO: Boise, July 13-15. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

INDIANA: *Examination.* Indianapolis, June 23-25. Ex. Sec., Miss Ruth V. Kirk, 538 K of P Bldg., Indianapolis.

IOWA:* *Examination.* Iowa City, June 15-17. Sec., Dr. M. A. Royal, 506 Fleming Bldg., Des Moines.

KANSAS: Kansas City, June 10-11. Sec., Dr. O. W. Davidson, 864 New Brotherhood Bldg., Kansas City.

KENTUCKY: *Examination.* Louisville, June 8-10. Sec., Dr. Bruce Underwood, 620 South Third St., Louisville 2.

LOUISIANA: *Examination.* New Orleans, June 4-6. Sec., Dr. Roy B. Harrison, 1507 Hibernia Bank Bldg., New Orleans.

MAINE: *Reciprocity and Examination.* Augusta, July 14-15. Sec., Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Examination.* Baltimore, June 16-19. Sec., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore 1.

MASSACHUSETTS: *Examination.* Boston, July 14-17. Sec., Dr. Robert C. Cochrane, Room 37, State House, Boston 33.

MICHIGAN: *Examination.* June 10-12 (tentative), Ann Arbor and Detroit. Sec., Dr. J. Earl McIntyre, 201-4 Hollister Bldg., Lansing.

MINNESOTA:* Minneapolis, April 21-23. Sec., Dr. J. F. DuBois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MISSISSIPPI: Jackson, June 22-24. Sec., Dr. Felix J. Underwood, Old Capitol Bldg., Jackson 113.

NEBRASKA:* *Examination.* Omaha, June 15-17. Director, Mr. Husted K. Watson, Room 1009 State Capitol Bldg., Lincoln 9.

NEW JERSEY: Trenton, June 16-19. Sec., Dr. Earl S. Hallinger, 28 West State St., Trenton.

NORTH CAROLINA: *Reciprocity.* Pinehurst, May 11. *Examination.* Raleigh, June 22-25. *Reciprocity.* Raleigh, June 23. Sec., Dr. Joseph J. Combs, 716 Professional Bldg., Raleigh.

NORTH DAKOTA: Grand Forks, July 8-11. Sec., Dr. C. J. Glaspel, Grafton.

OHIO: *Examination.* Columbus, June 15-17. *Reciprocity.* Columbus, April 7. Sec., Dr. H. M. Platter, 21 W. Broad, Columbus 15.

OKLAHOMA:* *Examination.* Oklahoma City, June 10-11. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON:* *Examination.* Portland, July. *Reciprocity.* Portland, April 10-11. Exec. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg, Portland.

PENNSYLVANIA: *Examination.* Philadelphia and Pittsburgh, July. Act. Sec., Mrs. Margaret G. Steiner, Box 911, Harrisburg.

SOUTH DAKOTA:* Rapid City, June 17-18. Exec. Sec., Mr. John C. Foster, 300 1st National Bank Bldg., Sioux Falls.

TEXAS:* Fort Worth, June 22-24. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Ft. Worth 2.

UTAH: *Examination.* Salt Lake City, July. Asst. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City.

VIRGIN ISLANDS: *Examination.* St. Thomas, June 10-11. Sec., Dr. Earle M. Rice, Box 8, St. Thomas.

VIRGINIA: *Examination and Reciprocity.* Richmond, June 17-20. Address: Secretary, Board of Medical Examiners, 631 First St. S.W., Roanoke.

WISCONSIN:* *Reciprocity.* Oshkosh, April 23. *Examination.* Milwaukee, July 14-16. Sec., Dr. A. G. Koehler, 46 Washington Blvd., Oshkosh.

WYOMING: *Oral. Reciprocity.* Cheyenne, June 8. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ALASKA: On application. Juneau or other towns in Territory as decided by Board. *Reciprocity.* On application. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

ARKANSAS: *Examination.* Little Rock, May 5-6. Sec., Mr. Louis E. Gebauer, 1002 Donaghey Bldg., Little Rock.

DISTRICT OF COLUMBIA: *Examination.* Washington, April 20-21. Commissioner of Licensure, Dr. Daniel L. Seckinger, 4130 East Municipal Bldg., Washington.

FLORIDA: *Examination.* Gainesville, June 6. Sec., Mr. M. W. Emmel, Box 340, University of Florida, Gainesville.

NEBRASKA: Omaha, May 5-6. Director, Bureau of Examining Boards, Mr. Husted K. Watson, Room 1009, State Capitol Bldg., Lincoln 9.

SOUTH DAKOTA: *Examination.* Vermillion, June 5-6. Sec., Dr. Gregg M. Evans, 310 E. 15th St., Yankton.

WASHINGTON: *Examination.* Seattle, July 8-9. Sec., Department of Licenses, Mr. Edward C. Dohm, Olympia.

WISCONSIN: *Examination.* Milwaukee, June 13. Final date for filing application is June 6. Sec., Dr. W. H. Barber, 621 Ransom St., Ripon.

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* Basic Science Certificate required.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. George F. Lull, 535 North Dearborn St., Chicago 10, Secretary.

1953 Annual Session, New York, June 1-5.

1953 Clinical Session, St. Louis, Dec. 1-4.

1954 Annual Session, San Francisco, June 21-25.

1954 Clinical Session, Miami, Florida, Nov. 30-Dec. 3.

AERO MEDICAL ASSOCIATION, Biltmore Hotel, Los Angeles, May 11-13. Dr. Thomas H. Sutherland, P. O. Box 26, Marion, Ohio, Secretary.

AMERICAN ACADEMY OF PEDIATRICS, Areal Meeting, Hotel Statler, Boston, April 20-22. Dr. E. H. Christopherson, 610 Church St., Evanston, Illinois, Executive Secretary.

AMERICAN ACADEMY OF TUBERCULOSIS PHYSICIANS, Hotel Roosevelt, New York, May 30. Dr. Oscar S. Levin, P. O. Box 7011, Denver 6, Secretary.

AMERICAN ASSOCIATION FOR CLEFT PALATE REHABILITATION, The Atlanta-Biltmore, Atlanta, Ga., April 27-28. Dr. Jack Matthews, 1617 Cathedral of Learning, University of Pittsburgh, Pittsburgh 13, Secretary.

AMERICAN ASSOCIATION OF GENITO-URINARY SURGEONS, The Homestead, Hot Springs, Va., May 6-8. Dr. Norris J. Heckel, 122 S. Michigan Blvd., Chicago 3, Secretary.

AMERICAN ASSOCIATION ON MENTAL DEFICIENCY, Hotel Statler, Los Angeles, May 12-16. Dr. Neil A. Dayton, P. O. Box 96, Willimantic, Conn., Secretary.

AMERICAN ASSOCIATION FOR THE STUDY OF NEOPLASTIC DISEASES, Lord Baltimore Hotel, Baltimore, April 30-May 2. Dr. Bruce H. Sisler, Gatlinburg, Tenn., Secretary.

AMERICAN BLOOD IRRADIATION SOCIETY, Waldorf-Astoria, New York, May 30-31. Dr. H. T. Lewis, 1241 Peermont Ave., Pittsburgh, Secretary.

AMERICAN BRONCHO-ESOPHAGOLOGICAL ASSOCIATION, Roosevelt Hotel, New Orleans, April 28-29. Dr. Edwin N. Broyles, 1100 North Charles St., Baltimore 1, Secretary.

AMERICAN COLLEGE OF ALLERGISTS, Conrad Hilton Hotel, Chicago, April 26-29. Dr. Fred W. Wittich, 423 LaSalle Medical Bldg., Minneapolis 2, Secretary.

AMERICAN COLLEGE OF CARDIOLOGY, Hotel Statler, Washington, D. C., June 7-9. Dr. Philip Reichert, 480 Park Ave., New York 22, Secretary.

AMERICAN COLLEGE OF CHEST PHYSICIANS, Hotel New Yorker, New York, May 28-31. Mr. Murray Kornfeld, 112 East Chestnut St., Chicago 11, Executive Director.

AMERICAN DERMATOLOGICAL ASSOCIATION, Lake Placid Club, Lake Placid, N. Y., June 9-13. Dr. Louis A. Brunsting, 102 Second Ave. S.W., Rochester, Minn., Secretary.

AMERICAN DIABETES ASSOCIATION, Hotel Commodore, New York, May 30-31. Dr. John A. Reed, 11 West 42d St., New York 36, Secretary.

AMERICAN FEDERATION FOR CLINICAL RESEARCH, Haddon Hall, Atlantic City, N. J., May 3. Dr. Lawrence E. Hinkle Jr., 525 East 68th St., New York 21, Secretary.

AMERICAN GASTRO-ENTEROLOGICAL ASSOCIATION, Claridge Hotel, Atlantic City, N. J., May 1-2. Dr. H. Marvin Pollard, University Hospital, Ann Arbor, Mich., Secretary.

AMERICAN GERIATRICS SOCIETY, Hotel Commodore, New York, May 28-30, Dr. Malford W. Thewlis, 25 Mechanic St., Wakefield, R. I., Secretary.

AMERICAN GOITER ASSOCIATION, Drake Hotel, Chicago, May 7-9. Dr. George C. Shivers, 100 E. St. Vrain St., Colorado Springs, Colo., Secretary.

AMERICAN MEDICAL WOMEN'S ASSOCIATION, Barbizon-Plaza Hotel, New York, May 29-31. Dr. Elizabeth R. Fischer, 10848 South Fairfield Ave., Chicago 43, Secretary.

AMERICAN LARYNGOLOGICAL ASSOCIATION, Roosevelt Hotel, New Orleans, April 26-27. Dr. Harry P. Schenck, 326 South 19th St., Philadelphia 3, Secretary.

AMERICAN LARYNGOLOGICAL, RHINOLOGICAL AND OTOLOGICAL SOCIETY, Roosevelt Hotel, New Orleans, April 28-30. Dr. C. Stewart Nash, 277 Alexander St., Rochester, N. Y., Secretary.

AMERICAN OPHTHALMOLOGICAL SOCIETY, The Homestead, Hot Springs, Va., May 28-30. Dr. Maynard C. Wheeler, 30 West 59th St., New York 19, Secretary.

AMERICAN OTOLOGICAL SOCIETY, Roosevelt Hotel, New Orleans, May 1-2. Dr. John R. Lindsay, 950 East 59th Street, Chicago 37, Secretary.

AMERICAN PEDIATRIC SOCIETY, Hotel Traymore, Atlantic City, N. J., May 6-8. Dr. Aims C. McGuinness, 237 Medical Laboratories, University of Pennsylvania, Philadelphia 4, Secretary.

AMERICAN PROCTOLOGIC SOCIETY, Hotel Statler, Boston, June 10-13. Dr. Stuart T. Ross, 131 Fulton Ave., Hempstead, N. Y., Secretary.

AMERICAN PSYCHIATRIC ASSOCIATION, Hotel Statler, Los Angeles, May 4-9. Dr. R. Finley Gayle Jr., 6300 Three Chopt Road, Richmond, Va., Secretary.

AMERICAN RADIUM SOCIETY, Plaza Hotel, St. Louis, April 19-22. Dr. John E. Wirth, 635 Herkimer St., Pasadena 1, Calif., Secretary.

AMERICAN RHEUMATISM ASSOCIATION, Waldorf-Astoria, New York, May 28-29. Dr. William H. Kammerer, 33 East 61st St., New York 21, Secretary.

AMERICAN SOCIETY FOR CLINICAL INVESTIGATION, Chalfonte-Haddon Hall, Atlantic City, N. J., May 4. Dr. William M. M. Kirby, University of Washington School of Medicine, Seattle 5, Secretary.

AMERICAN SOCIETY OF MAXILLOFACIAL SURGEONS, Cleveland, April 26-29. Dr. Casper M. Epsteen, 25 East Washington St., Chicago 2, Secretary.

AMERICAN SOCIETY FOR THE STUDY OF STERILITY, Henry Hudson Hotel, New York, May 25-31. Dr. Walter W. Williams, 20 Magnolia Terrace, Springfield 8, Mass., Secretary.

AMERICAN THERAPEUTIC SOCIETY, The Biltmore, New York, May 28-31. Dr. Oscar B. Hunter Jr., 915 Nineteenth St. N.W., Washington 6, D. C., Secretary.

AMERICAN TRUDEAU SOCIETY, Hotel Statler, Los Angeles, May 18-22. Dr. John D. Steele, 1790 Broadway, New York 19, Secretary.

AMERICAN UROLOGICAL ASSOCIATION, Hotel Jefferson, St. Louis, May 11-14. Dr. Charles H. deT. Shivers, Boardwalk National Arcade Bldg., Atlantic City, N. J., Secretary.

ARIZONA MEDICAL ASSOCIATION, Pioneer Hotel, Tucson, April 26-30. Dr. D. W. Melick, 541 Security Bldg., Phoenix, Secretary.

ARKANSAS MEDICAL SOCIETY, Little Rock, April 20-22. Dr. J. J. Monfort, 215 Kelley Bldg., Fort Smith, Secretary.

ASSOCIATION OF AMERICAN PHYSICIANS, Haddon Hall, Atlantic City, N. J., May 5-6. Dr. W. Barry Wood Jr., 600 S. Kingshighway Blvd., St. Louis 10, Secretary.

CALIFORNIA MEDICAL ASSOCIATION, Biltmore Hotel, Los Angeles, May 24-28. Dr. Albert C. Daniels, 450 Sutter St., San Francisco 8, Secretary.

CATHOLIC HOSPITAL ASSOCIATION OF THE UNITED STATES AND CANADA, Kansas City, Mo., May 25-28. Rev. John J. Flanagan, S.J., 1438 South Grand Blvd., St. Louis 4, Director.

CONFERENCE OF PRESIDENTS AND OTHER OFFICERS OF STATE MEDICAL ASSOCIATIONS, New York, May 31. Mr. Thomas R. O'Brien, 634 North Grand Blvd., St. Louis 3, Secretary.

CONNECTICUT STATE MEDICAL SOCIETY, Hampden High School, New Haven, April 27-29. Dr. Creighton Barker, 160 St. Ronan St., New Haven, Secretary.

FLORIDA MEDICAL ASSOCIATION, Hollywood Beach Hotel, Hollywood, April 26-29. Dr. Samuel M. Day, 413 Professional Bldg., Jacksonville, Secretary.

GEORGIA, MEDICAL ASSOCIATION OF, Savannah, May 10-13. Dr. David H. Poer, 875 West Peachtree St. N.E., Atlanta, Secretary.

HAWAII TERRITORIAL MEDICAL ASSOCIATION, Island of Maui, April 30-May 3. Dr. Samuel L. Yee, 1163 South Beretania St., Honolulu, Secretary.

ILLINOIS STATE MEDICAL SOCIETY, Hotel Sherman, Chicago, May 19-22. Dr. Harold M. Camp, 224 South Main St., Monmouth, Secretary.

INDUSTRIAL MEDICAL ASSOCIATION, Los Angeles, April 21-24. Dr. Arthur K. Peterson, 350 East 22d St., Chicago 16, Secretary.

IOWA STATE MEDICAL SOCIETY, Des Moines, April 26-29. Dr. Allan B. Phillips, 529 36th St., Des Moines 12, Secretary.

KANSAS MEDICAL SOCIETY, Wichita, May 4-7. Dr. Dale D. Vermillion, 315 West Fourth St., Topeka, Secretary.

LOUISIANA STATE MEDICAL SOCIETY, Roosevelt Hotel, New Orleans, May 7-9. Dr. C. Grenes Cole, 1430 Tulane Ave., New Orleans 12, Secretary.

MARYLAND, MEDICAL AND CHIRURGICAL FACULTY OF THE STATE OF, Baltimore, April 28-29. Dr. George H. Yeager, 1211 Cathedral St., Baltimore 1, Secretary.

MASSACHUSETTS MEDICAL SOCIETY, Hotel Statler, Boston, May 19-21. Dr. Robert W. Buck, 22 The Fenway, Boston 15, Acting Secretary.

MINNESOTA STATE MEDICAL ASSOCIATION, Hotel St. Paul, St. Paul, May 25-27. Dr. B. B. Souster, 496 Lowry Medical Arts Bldg., St. Paul 2, Secretary.

MISSISSIPPI STATE MEDICAL ASSOCIATION, Biloxi, May 11-14. Mr. Roland B. Kennedy, 508 First Federal Bldg., Jackson, Executive Secretary.

MISSOURI STATE MEDICAL ASSOCIATION, Kansas City, April 26-29. Dr. H. E. Petersen, 634 N. Grand Blvd., St. Louis 3, Secretary.

NATIONAL TUBERCULOSIS ASSOCIATION, Statler and Biltmore hotels, Los Angeles, May 18-22. Mr. Kemp D. Battle, 1790 Broadway, New York 19, Secretary.

NEBRASKA STATE MEDICAL ASSOCIATION, Paxton Hotel, Omaha, May 11-14. Dr. R. B. Adams, 1315 Sharp Bldg., Lincoln 8, Secretary.

NEW JERSEY, MEDICAL SOCIETY OF, Haddon Hall, Atlantic City, May 18-21. Dr. Marcus H. Greifinger, 315 West State St., Trenton 8, Secretary.

NEW MEXICO MEDICAL SOCIETY, Hilton Hotel, Albuquerque, May 7-9. Dr. T. E. Kircher Jr., 221 West Central Ave., Albuquerque, Secretary.

NEW YORK, MEDICAL SOCIETY OF THE STATE OF, Hotel Statler, Buffalo, May 4-8. Dr. Walter P. Anderton, 386 Fourth Avenue, New York 16, Secretary.

NORTH CAROLINA, MEDICAL SOCIETY OF THE STATE OF, Hotel Carolina, Pinehurst, May 10-13. Dr. Millard D. Hill, 203 Capital Club Bldg., Raleigh, Secretary.

NORTH DAKOTA STATE MEDICAL ASSOCIATION, Clarence Parker Hotel, Minot, May 9-12. Dr. E. H. Boerth, Box 1198, Bismarck, Secretary.

OGDEN SURGICAL SOCIETY, Orpheum Theater, Ogden, Utah, May 20-22. Dr. Irwin B. McQuarrie, 401 Eccles Bldg., Ogden, Utah, President.

OHIO STATE MEDICAL ASSOCIATION, Netherland Plaza, Cincinnati, April 21-23. Mr. Charles S. Nelson, 79 East State St., Columbus 15, Executive Secretary.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY, Los Angeles, May 24-28, Dr. H. P. House, 1136 West 8th St., Los Angeles 14, Secretary.

RHODE ISLAND MEDICAL SOCIETY, Providence, May 6-7. Dr. Thomas Perry Jr., 106 Francis Street, Providence, Secretary.

SECTIONAL MEETINGS, AMERICAN COLLEGE OF SURGEONS:

CALGARY, Alberta, Canada, Palliser Hotel, April 23-24. Dr. Donald G. MacQueen, Colonel Belcher Hospital, Calgary, Alberta, Canada, Chairman.

SOCIETY OF BIOLOGICAL PSYCHIATRY, Hotel Statler, Los Angeles, May 3. Dr. George N. Thompson, 2010 Wilshire Blvd., Los Angeles 5, Secretary.

SOCIETY OF CLINICAL SURGERY, Spring Meeting, Nashville, Tenn., May 1-2. Dr. Champ Lyons, 620 South 20th St., Birmingham 5, Ala., Secretary.

SOCIETY FOR INVESTIGATIVE DERMATOLOGY, Belmont Plaza Hotel, New York, May 30-31. Dr. Herman Beerman, 255 South 17th St., Philadelphia 3, Secretary.

SOCIETY FOR PEDIATRIC RESEARCH, Hotel Traymore, Atlantic City, N. J., May 4-6. Dr. Sydney S. Gellis, 330 Brookline Ave., Boston 15, Secretary.

SOCIETY FOR VASCULAR SURGERY, Hotel Pierre, New York, May 31. Dr. George D. Lilly, 25 S.E. Second Ave., Miami 32, Fla., Secretary.

SOUTH CAROLINA MEDICAL ASSOCIATION, Columbia Hotel, Columbia, May 4-7. Dr. Robert Wilson Jr., 120 W. Cheves St., Florence, Secretary.

SOUTHEASTERN ALLERGY ASSOCIATION, Andrew Jackson Hotel, Nashville, Tenn., May 15-16. Dr. Katharine B. MacInnis, 1515 Bull St., Columbia 1, S. C., Secretary.

SOUTHERN OREGON MEDICAL SOCIETY, Oregon Caves Chateau, Oregon Caves, Ore., June 10. Dr. R. Ray Johnson, Grants Pass, Ore., Secretary.

TEXAS MEDICAL ASSOCIATION, Shamrock Hotel, Houston, April 26-29. Mr. N. C. Forrester, 1801 Lamar Blvd., Austin, Executive Secretary.

THE ENDOCRINE SOCIETY, Hotel Statler, New York, May 28-30. Dr. Henry H. Turner, 1200 North Walker St., Oklahoma City 3, Secretary.

U. S. CHAPTER, INTERNATIONAL COLLEGE OF SURGEONS, SURGICAL DIVISION MEETINGS:

KNOXVILLE, TENN., Andrew Johnson Hotel, April 24-25. Dr. E. Park Niceley, Acuff Clinic, 514 West Church St., Knoxville, Tenn., Chairman.

CHICAGO, Congress Hotel, May 5-6. Dr. Karl A. Meyer, 30 North Michigan Ave., Chicago 2, Chairman.

WESTERN INDUSTRIAL MEDICAL ASSOCIATION, Hotel Statler, Los Angeles, April 18-25. Dr. E. P. Luongo, General Petroleum Corp., 613 South Flower St., Los Angeles 14, Secretary.

WESTERN SECTION AMERICAN UROLOGICAL ASSOCIATION, Palace Hotel, San Francisco, April 27-30. Dr. A. A. Kutzmann, 1930 Wilshire Blvd., Los Angeles 5, Secretary.

WESTERN SOCIETY OF ELECTRO-ENCEPHALOGRAPHY, Hotel Statler, Los Angeles, May 9-10. Dr. Sylvester N. Berens, 902 Boren Ave., Seattle, Secretary.

FOREIGN

BRITISH MEDICAL ASSOCIATION, Cardiff, S. Wales, July 13-17. Dr. A. MaCrae, B. M. A. House, Tavistock Square, London W.C.1, England, Secretary.

CANADIAN MEDICAL ASSOCIATION, Winnipeg, Manitoba, Canada, June 15-19. Dr. T. C. Routley, 135 St. Clair Avenue W., Toronto 5, Ontario, Canada, General Secretary.

CONGRESS OF INTERNATIONAL ANESTHESIA RESEARCH SOCIETY, Chateau Frontenac, Quebec, Canada, October 26-29. Dr. A. William Friend, 515 Nome Ave., Akron 20, Ohio, Chairman, Program Committee.

CONGRESS OF INTERNATIONAL LEAGUE AGAINST RHEUMATISM, Geneva and Zurich, Switzerland, Aug. 24-29. For information write: Dr. W. Tegner, The London Hospital, London E.1, England.

CONGRESS OF THE INTERNATIONAL SOCIETY OF ANGIOLOGY, Lisbon, Portugal, Sept. 18-20. Dr. Henry Haimovici, 105 East 90th St., New York 28, N. Y., U. S. A., Secretary.

CONGRESS OF THE INTERNATIONAL SOCIETY OF SURGERY, Lisbon, Portugal, Sept. 14-20. Dr. L. Dejardin, 141, rue Belliard, Brussels, Belgium, General Secretary.

EUROPEAN CONGRESS OF ALLERGOLOGY, Copenhagen, Denmark, May 20-23. Dr. Egon Brunn, Gersonavej 8, Hellerup, Copenhagen, Denmark, Secretary General.

INTERNATIONAL CONFERENCE ON THROMBOSIS AND EMBOLISM, Basle, Switzerland, July 15-19, 1954. Dr. W. Merz, Chief Medical Officer, Gynecological Clinic, University of Basle, Basle, Switzerland, Hon. Secretary.

INTERNATIONAL CONGRESS OF AUDIOLOGY, Leiden, Netherlands, June 5-6. Dr. H. A. E. ve Dishoeck, Leiden University, Leiden, Netherlands, President.

INTERNATIONAL CONGRESS OF ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY, Boston, Mass., U. S. A., Aug. 18-21. Dr. Robert S. Schwab, Massachusetts General Hospital, Boston 14, Mass., U. S. A., Secretary-General.

INTERNATIONAL CONGRESS OF THE EUROPEAN SOCIETY OF HAEMATOLOGY, Amsterdam, Holland, Sept. 8-12. Dr. M. C. Verloop, Maliesingle 15, Utrecht, Holland, Secretary.

INTERNATIONAL CONGRESS ON GENETICS, Bellagio, Italy, August 4. Prof. C. Barigozzi, Instituto de Genetica, Universita de Milano, 10 via Celoria, Milan, Italy, Secretary.

INTERNATIONAL CONGRESS OF GYNECOLOGY, Geneva, Switzerland, July 21-26, 1954. Dr. Maurice Fabre, 1, rue Jules-Lefebore, Paris IXe, France, General Secretary.

INTERNATIONAL CONGRESS OF HIPPOCRATIC MEDICINE, Evian, France, Sept. 3-6. Prof. P. Delore, 13 rue Jarente, Lyons, France, Secretary-General.

INTERNATIONAL CONGRESS FOR HISTORY OF SCIENCE, Jerusalem, Israel, August 3-7. Prof. F. S. Bodenheimer, Hebrew University, Jerusalem, Israel, President.

INTERNATIONAL CONGRESS OF INTERNATIONAL COLLEGE OF SURGEONS, Sao Paulo, Brazil, April 26-May 2, 1954. Dr. Max Thorek, 1516 Lake Shore Drive, Chicago, Illinois, U.S.A., Secretary-General.

INTERNATIONAL CONGRESS OF LOGOPEDICS AND PHONIATRICS, Milan and Stresa, Italy, Sept. 1-7. Dr. Deso A. Weiss, 115 East 86th St., New York 28, N. Y., U. S. A., General Secretary.

INTERNATIONAL CONGRESS ON MEDICAL LIBRARIANSHIP, London, England, July 20-25. Mr. W. R. LeFanu, % London School of Hygiene and Tropical Medicine, Keppel Street, London, W.C.1, England, Chairman.

INTERNATIONAL CONGRESS ON MENTAL HEALTH, University of Toronto, Toronto, Ontario, Canada, Aug. 14-21, 1954. For information write: Executive Officer, International Congress on Mental Health, 111 St. George St., Toronto, Ontario, Canada.

INTERNATIONAL CONGRESS OF MICROBIOLOGY, Rome, Italy, Sept 6-12. For information write: Dr. V. Puntoni, Citta Universitaria, Rome, Italy.

INTERNATIONAL CONGRESS ON OBSTETRICS AND GYNECOLOGY, Geneva, Switzerland, July 20-24, 1954. For information write: Prof. H. de Watteville, Maternité Hôpital Cantonal, Geneva, Switzerland.

INTERNATIONAL CONGRESS OF OTO-NEURO-OPHTHALMOLOGY, Bologna, Italy, May 3-7. Dr. Guiseppe Cristini, Clinica Oculistica, Policlinico, Bologna, Italy, General Secretary.

INTERNATIONAL CONGRESS OF OTORHINOLARYNGOLOGY, Amsterdam, Netherlands, June 8-13. Dr. W. H. Struben, J. J. Viottastraat 1, Amsterdam, Netherlands, Secretary.

INTERNATIONAL CONGRESS OF PAEDIATRICS, Havana, Cuba, Oct. 12-17. Prof. Felix Hurtado, 5a Avenue 124, Miramar, Havana, Cuba, President.

INTERNATIONAL CONGRESS OF RADIOLOGY, Copenhagen, Denmark, July 19-25. Professor Flemming Norgaard, 10 Oster Voldgade, Copenhagen K, Denmark, Secretary General.

INTERNATIONAL CONGRESSES OF TROPICAL MEDICINE AND MALARIA, Istanbul, Turkey, Aug. 28-Sept. 4. Professor Dr. Ihsan Sükrü Aksel, Tunel Meydam, Beyoglu, Istanbul, Turkey, General Secretary.

INTERNATIONAL CONVENTION OF X-RAY TECHNICIANS, Royal York Hotel, Toronto, Canada, June 28-July 2. For information write: Miss Beatrice Hurley, R.T., Registrar, St. Catherine Hospital, East Chicago, Ind., U. S. A.

INTERNATIONAL FERTILITY ASSOCIATION, Henry Hudson Hotel, New York, N. Y., U. S. A., May 25-31. Dr. Abner I. Weisman, 1160 Fifth Avenue, New York 29, N. Y., U. S. A., Associate Secretary General.

INTERNATIONAL GERONTOLOGICAL CONGRESS, London and Oxford, England, July 12-22, 1954. Prof. R. E. Tunbridge, General Infirmary, Department of Medicine, The University, Leeds, England, President.

INTERNATIONAL GYNAECOLOGICAL MEETING, Paris, France, May 22-23. For information write: Dr. Jacques Courtois, 1, rue Racine, St. Germain-en-Laye, Seine et Oise, France.

INTERNATIONAL HOSPITAL CONGRESS, London, England, May 25-30. Capt. J. E. Stone, 10 Old Jewry, London, EC2, England, Hon. Secretary.

INTERNATIONAL LEPROSY CONGRESS, Madrid, Spain, Oct. 3-10. Dr. Felix Contreras, Moreto 15, Madrid, Spain, Secretary.

INTERNATIONAL PHYSIOLOGICAL CONGRESS, Montreal, Canada, Aug. 31-Sept. 4. Dr. A. S. V. Burgen, Dept. of Physiology, McGill University, Montreal, Canada, Secretary.

INTERNATIONAL PSYCHO-ANALYTICAL CONGRESS, Bedford College, Regent's Park, London N.W.1, England, July 26-30. Dr. Ruth S. Eissler, 285 Central Park West, New York 24, N. Y., Hon. Secretary.

INTERNATIONAL VETERINARY CONGRESS, Stockholm, Sweden, Aug. 9-15. Prof. Axel Isaksson, Institute of Veterinary Medicine, Stockholm 50, Sweden, Secretary.

PACIFIC SCIENCE CONGRESS, Quezon City and Manila, Philippines, Nov. 16-28. Dr. Patrocinio Valenzuela, College of Pharmacy, University of the Philippines, Quezon City, Philippines, Secretary-General.

PAN AMERICAN CONGRESS OF THE MEDICAL PRESS, Buenos Aires, Argentine, July 12-16. Secretaria del Congress, 763 Uriburu, Buenos Aires, Argentine.

PHILIPPINE MEDICAL ASSOCIATION, Manila, April 19-26. Dr. Manuel D. Penas, Doctor's Hospital, 707 Vermont St., Manila, Philippines, Secretary.

ROYAL SANITARY INSTITUTE HEALTH CONGRESS, Hastings, England, April 28-May 1. For information write: Secretary, Royal Sanitary Institute, 90 Buckingham Palace Road, London 5, W1, England.

WORLD CONFERENCE ON MEDICAL EDUCATION, British Medical Association House, Tavistock Square, W.C.1, London, England, Aug. 22-29. Secretariat: World Medical Association, 2 East 103d St., New York 29, N. Y., U. S. A.

WORLD CONGRESS OF THE WORLD CONFEDERATION FOR PHYSICAL THERAPY, London, England, Sept. 7-12. Miss M. J. Neilson, Chartered Society of Physiotherapy, Tavistock House, South, Tavistock Square, London, W.C.1, England, Secretary.

WORLD MEDICAL ASSOCIATION, The Hague, Netherlands, Aug. 31-Sept. 7. Dr. Louis H. Bauer, 2 East 103d St., New York 29, N. Y., Secretary-General.

DEATHS

Brown, Edward Vail Lapham ⊕ Chicago; born in Morrison, Ill., Aug. 15, 1876; the Hahnemann Medical College and Hospital, Chicago, 1897; Rush Medical College, Chicago, 1898; studied in Berlin and Vienna; specialist certified by the American Board of Ophthalmology; professor emeritus of ophthalmology at the University of Chicago School of Medicine and clinical professor emeritus of ophthalmology at (Rush) University of Illinois College of Medicine; in 1942 the collegiate division of the University of Chicago awarded him an honorary citation in recognition of achievement in his special field; member and past president of the American Ophthalmological Society; member of the Association for Research in Ophthalmology; in 1951 won the Leslie Dana medal, a national award given annually for achievement in preventing blindness; president of the board of directors of the Provident Medical Associates when it was organized in 1946 and continued in that capacity when it changed its name in 1952 to National Medical Fellowships Inc., which awards fellowships and scholarships to Negroes in medicine; an honorary member of the Hungarian Ophthalmological Society and the Institute of Medicine of Chicago; chairman of the Mayor's Committee on Human Relations; a director of the Illinois Society for the Prevention of Blindness; president of the board at Hadley Correspondence School for the Blind in Winnetka, Ill.; served on the staffs of the Presbyterian and Cook County hospitals for many years; president of the board of trustees at the Provident Hospital at the time of his death; died at his home in Winnetka, Ill., March 1, aged 76, of carcinoma of the pancreas.

White, Joseph Hill ⊕ Medical Director, U. S. Public Health Service, retired, Washington, D. C.; born in Milledgeville, Ga., May 4, 1859; College of Physicians and Surgeons, Baltimore, 1883; in 1884 joined the U. S. Marine Hospital Service, now known as the Public Health Service; served in various ranks, including two terms as assistant surgeon-general from 1899 to 1903 and from 1920 to 1925 when he retired; in 1905 served in New Orleans during an extensive outbreak of yellow fever; served as vice-director of the international health board of the Rockefeller Foundation; detailed during World War I as general inspector and director of the antimalarial work for the U. S. Army with the rank of colonel; first chairman of the National Leprosy Commission; in 1920 a delegate from the United States to the sixth International Leprosy Conference; past president of the American Society of Tropical Medicine; chairman of the Section on Hygiene and Sanitary Science of the American Medical Association, 1908-1909; served as lecturer of tropical diseases and preventive medicine at the universities of Alabama and Tennessee; made grand officer of the Order of Quetzal by the government of Guatemala for distinguished service in yellow fever eradication in that country; died Feb. 28, aged 93, of senility.

Eubank, Ambrose Eastin ⊕ Independence, Mo.; born in Winchester, Ky., April 8, 1878; University Medical College of Kansas City, 1901; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; past president of the Jackson County Medical Society, which in 1946 presented him with the gold key of the society for his service to the society; formerly practiced in Kansas City, where he was assistant police surgeon, and on the staffs of the General, St. Mary's, and Menorah hospitals; died in the Research Hospital in Kansas City, Mo., Feb. 23, aged 74, of coronary disease.

Bell, Landes Hughes, Commander, U. S. Navy, retired, San Diego, Calif.; born in Warrensburg, Mo., July 9, 1909; University of Rochester School of Medicine and Dentistry, Rochester, N. Y., 1933; entered the medical corps of the U. S. Navy Aug. 20, 1937; was one of the early Navy-trained flight surgeons, and was on duty at Kaneohi Naval Air Station, Oahu, Territory of Hawaii, when the Japanese attacked that island Dec. 7, 1941; later spent 18 months on New Caledonia during the South Pacific fighting; retired March 29, 1952; affiliated with Mercy Hospital; died in the Naval Hospital Dec. 21, aged 43, of metastatic hypernephroma.

Plummer, William Ward ⊕ Buffalo; born in Buffalo Dec. 13, 1877; University of Buffalo School of Medicine, 1902; professor of orthopedic surgery emeritus at his alma mater; specialist certified by the American Board of Orthopaedic Surgery; member of the American Orthopaedic Association and the American Academy of Orthopaedic Surgeons, of which he was president; during World War II civilian consultant in orthopedics to the surgeon-general of the U. S. Army; affiliated with the Edward J. Meyer Memorial, Buffalo General, and Children's hospitals; died Feb. 16, aged 75, of cerebral vascular accident.

Ayme, Edward Lucien Emile ⊕ New York City; College of Physicians and Surgeons, medical department of Columbia College, New York, 1885; an officer in the medical corps of the U. S. Army during World War I; from 1934 to 1946 on the faculty of the New York Post-Graduate Medical School and Hospital; served on the staffs of the Roosevelt Hospital, Hospital for the Ruptured and Crippled, Post-Graduate Hospital, and Misericordia Hospital; wrote numerous articles for magazines on medical, religious, and philosophical subjects; contributor to the Catholic Encyclopedia; died Feb. 3, aged 90.

Bauer, William H., Sylvia, Kan.; Homeopathic Medical College of Missouri, St. Louis, 1896; for many years a member of the board of the state tuberculosis association; died Jan. 16, aged 82, of cerebral thrombosis.

Baysinger, Stuart Lee ⊕ Rolla, Mo.; Missouri Medical College, St. Louis, 1890; member of the House of Delegates of the American Medical Association, 1920-1921 and 1928-1932; for many years college physician for the school of mines; died Jan. 30, aged 83.

Bozenhardt, William Frederick ⊕ Ridgewood, N. Y.; Cornell University Medical College, New York, 1905; fellow of the American College of Surgeons; affiliated with Wyckoff Heights and Bethany Deaconess hospitals in Brooklyn; died Feb. 1, aged 69, of heart disease.

Brenholtz, Walter Scott ⊕ Williamsport, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1892; for many years secretary and at one time president of the Lycoming County Medical Society; formerly vice-president of the Medical Society of the State of Pennsylvania, of which he was a trustee, and councilor of the 10th district (12th and 15th censorial districts); affiliated with Williamsport Hospital; first editor of the *Medical Bulletin of Lycoming County;* died Feb. 8, aged 85, of arteriosclerosis.

Burke, Alexander William ⊕ Cameron, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1909; served during World War I; worked with the Rockefeller Institute in Africa and South America; formerly acting chief of the division of tuberculosis control for the Illinois Department of Public Health and district health superintendent for the five county areas designated as District 10; died March 6, aged 67.

Corbett, William Winand ⊕ San Diego, Calif.; Georgetown University School of Medicine, Washington, D. C., 1927; member of the Medical and Chirurgical Faculty of the State of Maryland and the Industrial Medical Association; for many years on the professional staff of the Council on Medical Education and Hospitals of the American Medical Association, doing field survey work in the New England states and Illinois, resigning in April, 1952; died in an automobile accident in Yuma, Ariz., Feb. 24, aged 49.

Davidson, James J., Rocky Gap, Va.; Medical College of Virginia, Richmond, 1904; died Dec. 31, aged 74, of uremia.

⊕ Indicates Member of the American Medical Association.

Dunlap, Wallace Asbury ✠ Des Moines, Iowa; Drake University College of Medicine, Des Moines, 1903; died Dec. 12, aged 74, of cerebral hemorrhage.

Egbert, Roy ✠ Indianapolis; State College of Physicians and Surgeons, Indianapolis, 1907; on the staff of Methodist Hospital, where he died Jan. 17, aged 70, of lobar pneumonia.

Ferber, Julius ✠ New York City; University and Bellevue Hospital Medical College, New York, 1912; affiliated with Goldwater Memorial Hospital and Manhattan General Hospital, where he died Feb. 6, aged 65.

Fetterman, Wilfrid Bernard ✠ Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1898; formerly on the faculty of the Woman's Medical College of Pennsylvania; served during World War I and was awarded the Croix de Guerre by France; at one time affiliated with Phipps Institute; died in Germantown Hospital Jan. 28, aged 75, of arteriosclerotic heart disease.

Glenn, LaFayette ✠ Ramsey, Ind.; Hospital College of Medicine, Louisville, Ky., 1903; affiliated with Floyd-Harrison Counties Health Board; on the staff of St. Edward's Hospital in New Albany; died Jan. 19, aged 76, of coronary thrombosis.

Good, Henry Lee, Hamilton, Ohio; Pulte Medical College, Homeopathic, Cincinnati, 1907; honorary life member of the board of directors of the Y. M. C. A.; died in Bokelia, near Fort Myers, Fla., Jan. 21, aged 72, of coronary occlusion.

Gray, Warner Augustine ✠ Metropolis, Ill.; Chicago Medical School, 1933; died Feb. 4, aged 50, as the result of a fall.

Greenman, Newton Henry ✠ Decatur, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1898; died in the Lake View Community Hospital, Paw Paw, Jan. 18, aged 79, of arteriosclerosis following a fracture of the hip.

Grogin, Paul Block ✠ Pittsburgh; University of Pittsburgh School of Medicine, 1911; specialist certified by the American Board of Otolaryngology; on the staff of the Montefiore Hospital; died Jan. 6, aged 65, of inoperable carcinoma of the body of the pancreas.

Kraft, John Eugene ✠ Rochester, N. Y.; University of Buffalo School of Medicine, 1916; served on the staffs of St. Mary's and Park Avenue hospitals; died Jan. 13, aged 63, of carcinoma of the lung.

Krall, Paul Morton ✠ Kansas City, Kan.; St. Louis University School of Medicine, 1912; for many years on the faculty of the University of Kansas School of Medicine; past president of the Wyandotte County Medical Society; served during World War I; on the staffs of the St. Margaret's, Bethany, and Providence hospitals; died Jan. 23, aged 68, of coronary occlusion.

Krueger, Arthur H. R. ✠ Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1906; for many years affiliated with Belmont Hospital; died Jan. 31, aged 69, of carcinoma of the liver.

Marien, Joseph Ernest, Fitchburg, Mass.; Boston University School of Medicine, 1930; affiliated with Burbank Hospital; died Dec. 26, aged 48, of coronary occlusion.

Mason, Francis Henry, Brewton, Ala.; Medical College of Alabama, Mobile, 1891; died Dec. 27, aged 84, of arteriosclerosis.

Mehrhof, Charles Hamilton ✠ Ontario, N. Y.; University of Rochester School of Medicine and Dentistry, Rochester, 1934; certified by the National Board of Medical Examiners; on the faculty of his alma mater; on the staff of Strong Memorial Hospital in Rochester, where he died Jan. 4, aged 42, of acute leukemia.

Miller, Benjamin Neely ✠ Hickory Grove, S. C.; University of the South Medical Department, Sewanee, Tenn., 1901; served on the staff of the York County Hospital in Rock Hill; died Nov. 25, aged 76, of myocarditis.

Miller, William Henry, Charleston, S. C.; Tufts College Medical School, Boston, 1911; died Jan. 16, aged 73, of carcinoma of the lung.

Milligan, John Davidson ✠ Pittsburgh; Bellevue Hospital Medical College, New York, 1876; fellow of the American College of Surgeons; died Jan. 15, aged 101.

Mitchell, Lewis Thayer, Lorain, Ohio; University of the South Medical Department, Sewanee, Tenn., 1898; for many years physician for the Allegheny County Workhouse at Blawnox, Pa.; served during World War I; died Jan. 25, aged 75, of cor pulmonale and pulmonary emphysema.

Mobley, H. A. ✠ Vienna, Ga.; Southern Medical College, Atlanta, 1887; past president and for many years treasurer of the Dooly County Medical Association; county physician; affiliated with Dooly County Hospital; died Jan. 2, aged 86, of arteriosclerotic heart disease.

Moore, Amos Foster ✠ Dixon, Ill.; Marion-Sims College of Medicine, St. Louis, 1895; affiliated with the Dixon Public Hospital; served as deputy county coroner; for many years district surgeon for the Chicago and Northwestern Railroad; died Jan. 2, aged 85, of coronary insufficiency and hypertension.

Paine, Charles Samuel ✠ Bristol, Vt.; University of Vermont College of Medicine, Burlington, 1932; died Dec. 3, aged 44, of coronary thrombosis.

Parrish, Paul Leonard ✠ Brooklyn; Bellevue Hospital Medical College, New York, 1898; an Associate Fellow of the American Medical Association; professor emeritus of clinical pediatrics at State University of New York College of Medicine at New York City; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; fellow of the American College of Physicians; consulting pediatrician, Methodist, Wyckoff Heights, and Brooklyn Eye and Ear hospitals; died Jan. 29, aged 76, of cirrhosis of the liver.

Pfafflin, Charles Abram ✠ Indianapolis; Medical College of Ohio, Cincinnati, 1893; an Associate Fellow of the American Medical Association; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; on the staff of the Methodist Hospital; died Dec. 30, aged 79, of cerebral thrombosis and hypertensive cardiovascular disease.

Pierce, Clarence Warner, Los Angeles; University of Southern California College of Medicine, Los Angeles, 1898; fellow of the American College of Surgeons; for two terms president of the city board of education; died Feb. 2, aged 81, of coronary thrombosis and arteriosclerosis.

Pierce, Helen Frances ✠ Plymouth, Mass.; Boston University School of Medicine, 1887; formerly member of the school committee; an honorary member of the staff of Jordan Hospital, where she died Feb. 6, aged 91, of an injury received in a fall, bronchopneumonia, and hypertensive heart disease.

Polk, Lonney Lee, Purvis, Miss.; Memphis (Tenn.) Hospital Medical College, 1902; at one time vice-president of the Mississippi State Medical Association; died in Whitfield Feb. 17, aged 81.

Powers, Lillian Delger ✠ San Rafael, Calif.; Cooper Medical College, San Francisco, 1904; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association, American Psychoanalytic Association, and the American Psychosomatic Society; formerly practiced in New York City, where she was an instructor at the New York Psychoanalytic Institute; died in Greenbrae Jan. 9, aged 86, of arteriosclerosis and pulmonary embolism.

Reberdy, George Joseph ✠ Detroit; Detroit College of Medicine, 1910; served on the staffs of the Harper and Providence hospitals; died Feb. 3, aged 67, of gangrene of the foot, diabetes mellitus, and general atherosclerosis.

Reynolds, Ralph Wilson ✠ Fayette, Ohio; University of Wooster Medical Department, Cleveland, 1910; died Feb. 18, aged 64, of acute coronary occlusion.

Richardson, Dalton ⊕ Austin, Texas; Medical College of Ohio, Cincinnati, 1894; past president and secretary of the Travis County Medical Society; served as president of the Seventh District Medical Society and the Texas Radiological Society; fellow emeritus of the American College of Radiology and a member emeritus of the Radiological Society of North America; died Jan. 15, aged 84, of arteriosclerosis.

Richardson, Garwood Colvin ⊕ Chicago; Northwestern University Medical School, Chicago, 1922; assistant professor of obstetrics and gynecology at his alma mater; fellow of the American College of Surgeons; affiliated with Wesley Memorial Hospital, where he died March 4, aged 55, of myocardial infarction.

Ridley, Frank M. Jr., La Grange, Ga.; Atlanta College of Physicians and Surgeons, 1906; served on the state board of medical examiners and the state welfare board; died in City-County Hospital Jan. 28, aged 69.

Riordan, Arthur Hatton ⊕ Longmeadow, Mass.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1915; fellow of the American College of Surgeons; served during World War I; past president of the Hampden District Medical Society; consulting surgeon, Ludlow (Mass.) Hospital and Wing Memorial Hospital in Palmer; for many years affiliated with Mercy Hospital; died Feb. 13, aged 61, of coronary disease.

Robertson, William W. ⊕ Danville, Va.; College of Physicians and Surgeons, Baltimore, 1890; Bellevue Hospital Medical College, New York, 1891; died Jan. 19, aged 86.

Rosson, Charles Tilden Jr. ⊕ Hanford, Calif.; University of California Medical School, San Francisco, 1931; fellow of the American College of Surgeons; served during World War II; on the staff of General Hospital of Kings County; died Feb. 3, aged 47, of carcinoma of the esophagus.

Rutledge, Guy Dawson ⊕ Kaysville, Utah; St. Louis College of Physicians and Surgeons, 1910; died Feb. 5, aged 70.

Salomonsky, George Howard ⊕ Roanoke, Va.; Medical College of Virginia, Richmond, 1931; associated with the Veterans Administration until his retirement in 1952; died in the Memorial and Crippled Children's Hospital, Feb. 5, aged 49, of myocardial insufficiency.

Sevensma, Arthur R., Grand Rapids, Mich.; Detroit College of Medicine, 1907; died in the Butterworth Hospital Feb. 1, aged 77, of cerebral hemorrhage.

Smykowski, Bronislaw L. ⊕ Bridgeport, Conn.; Baltimore Medical College, 1911; past president of the Bridgeport Medical Society; formerly on the city welfare board and president of the city board of health; served as member of the board of trustees of Middletown (Conn.) State Hospital; affiliated with St. Vincent's Hospital, where he died Feb. 4, aged 69, of cerebral hemorrhage and right hemiplegia.

Spivey, William Lee, Los Angeles; Baylor University College of Medicine, Dallas, Texas, 1936; served during World War II; formerly affiliated with Hollywood Presbyterian Hospital; died in Arabia Jan. 3, aged 49, of coronary disease.

Starley, William Fletcher ⊕ Galveston, Texas; University of Texas School of Medicine, Galveston, 1895; died Feb. 19, aged 80.

Stoddard, Mortimer Joseph ⊕ Springfield, Mass.; University of Vermont College of Medicine, Burlington, 1898; an Associate Fellow of the American Medical Association; served during World War I; affiliated with Springfield Hospital, where he was president of the staff in 1935-1936; died Feb. 22, aged 78, of coronary thrombosis.

Stoneham, Hartwell Graham, Waverly, Va.; University of Maryland School of Medicine, Baltimore, 1913; served during World War I; died in Richmond Jan. 12, aged 65, of heart disease.

Strauss, Spencer Goldsmith ⊕ New York City; Columbia University College of Physicians and Surgeons, New York, 1913; served during World War I; formerly on the staff of the Lenox Hill Hospital, where he died Feb. 14, aged 65, of heart failure.

Taylor, Roy Nuseum ⊕ Riverside, Calif.; University of Tennessee College of Medicine, Memphis, 1924; fellow of the American Academy of Pediatrics; secretary of the Southwestern Pediatrics Association; served during World War I; medical officer and deputy health officer, Riverside County Health Department; on the attending staff of General Hospital of Riverside County; died Dec. 20, aged 56, of coronary thrombosis.

Thompson, George E. ⊕ Spartanburg, S. C.; Atlanta College of Physicians and Surgeons, 1901; formerly vice-president of the South Carolina Medical Association; died Jan. 13, aged 72, of a heart attack.

Thompson, Pauline A., Kansas City, Mo.; Barnes Medical College, St. Louis, 1905; died Feb. 23, aged 82, of arteriosclerosis.

Van Bibber, Armfield Franklin ⊕ Bel Air, Md.; University of Maryland School of Medicine, Baltimore, 1896; at one time vice-president of the Medical and Chirurgical Faculty of the State of Maryland; on the staff of the Harford Memorial Hospital in Havre de Grace; died in Church Home and Hospital in Baltimore, Jan. 16, aged 80, of bronchopneumonia.

Waller, William Ferrier ⊕ Angola, Ind.; Detroit College of Medicine, 1908; died in San Mateo, Calif., Feb. 9, aged 71, of pneumonia.

Ward, Walter Rowland ⊕ Birmingham, Ala.; Chattanooga Medical College, 1900; died in the Jefferson-Hillman Hospital Feb. 16, aged 76, of arteriosclerotic heart disease.

Wareham, Arthur ⊕ Morrisville, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1901; served during Spanish-American War; died Jan. 24, aged 76, of carcinoma of the left lung.

Weber, William Louis ⊕ Los Angeles; University of Southern California School of Medicine, Los Angeles, 1908; fellow of the American College of Surgeons; for many years chief surgeon for the Pacific Electric Railway; on the staff of St. Vincent's Hospital; died in the Duke Hospital, Durham, N. C., Jan. 30, aged 67, of hypertensive cardiovascular disease.

Wheeler, Morris Sheppard ⊕ Austin, Texas; University of Texas School of Medicine, Galveston, 1930; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; served during World War II; died in the VA Hospital, McKinney, Feb. 4, aged 49, of carcinoma of the lung.

Whitaker, Harry Osborn ⊕ Dublin, Ohio; Cleveland Homeopathic Medical College, 1901; served during World War I; formerly mayor and justice of the peace; died Feb. 16, aged 77, of a heart attack.

Wilkerson, William Washington ⊕ Montgomery, Ala.; Tulane University of Louisiana School of Medicine, New Orleans, 1919; died Feb. 12, aged 59.

Williams, Alonzo Jedson, Shawnee, Okla. (licensed on diploma or by years of practice); served during World War I; died in VA Hospital, Oklahoma City, Nov. 9, aged 73, of cerebral arteriosclerosis.

Wilson, Russell Conwell ⊕ Franklin, Ind.; Indiana University School of Medicine, Indianapolis, 1926; examiner for the Equitable Life Insurance Company; died Feb. 28, aged 57, of acute coronary occlusion.

Winham, Arthur Jerome Jr. ⊕ Wayne, Pa.; Jefferson Medical College of Philadelphia, 1942; served during World War II; affiliated with Pennsylvania Hospital in Philadelphia; died Dec. 30, aged 37.

Withers, Matthew William ⊕ Joliet, Ill.; Meharry Medical College, Nashville, Tenn., 1918; died Jan. 1, aged 60, of acute myocardial failure.

Zucker, Ernest ⊕ Newfield, N. Y.; Medizinische Fakultät der Universität, Vienna, Austria, 1925; died in Tompkins County Memorial Hospital, Ithaca, Jan. 10, aged 51, of lymphosarcoma.

GOVERNMENT SERVICES

NAVY

Assignments Available in Research Programs.—The Surgeon General of the Navy, Rear Adm. Lamont Pugh, in a recent directive, invited attention of qualified medical and dental officers to availability of assignments in the Navy's Medical Department Research Program. Medical and dental officers with special aptitude, training, experience, or inclination for research may apply by letter to the Bureau of Medicine and Surgery for assignment in research. The request should state the applicant's special qualifications and field of interest. Every effort will be made to place approved applicants seeking a career in research in appropriate activities for on-the-job training to further their advancement by postgraduate training in civilian institutions and to afford those who desire and demonstrate their competence a continuous career in research. The Navy has excellent facilities for research in the basic biological sciences, experimental medicine and surgery, dentistry, preventive and tropical medicine, aviation medicine, submarine and diving medicine, field and combat medicine, and the preventive medicine aspects of chemical, biological, and atomic warfare.

AIR FORCE

New Commandant of Air Force Medical School.—After four years as commandant of the Air Force School of Aviation Medicine, Randolph Field, Texas, Brig. Gen. Otis O. Benson Jr. has been assigned to the Surgeon General's Office in Washington, as chief of medical staffing and education. His successor will be Brig. Gen. Edward J. Kendricks, who is now in the post that General Benson will assume. Since General Benson assumed his command, planning has gone forward under his supervision on a projected 30 million dollar aeromedical center for the Air Force. Congress last year authorized the expenditure of 8 million dollars for construction of the first units of this center at Brooks Air Force Base near San Antonio, replacing the inadequate classrooms and laboratories that the school now occupies at Randolph Field. General Benson's war record included assignments as assistant surgeon of the North African Air Force, surgeon of the 15th Air Force, and surgeon of the Air Forces in the Mediterranean. After the war, he was chief of medical research in the office of the Air Surgeon in Washington. He received the John Jeffries award from the Institute of Aeronautical Sciences in 1950.

DEPARTMENT OF DEFENSE

Medicomilitary Symposium at Great Lakes, Illinois.—The combined armed services will hold a medicomilitary symposium at the Naval Hospital, Great Lakes, Illinois, May 6-8. Among those on the program will be the three Surgeons General and the medical director of the Veterans Administration. There will be a panel on medical reserve problems in which the Surgeons General will take part and in which questions will be asked from the floor. Dr. Melvin A. Casberg on Wednesday will speak on "Armed Forces Medicine and the Department of Defense," and Eugene Zuckert of the Atomic Energy Commission on "Where We Stand in 1953." On Thursday, Major Solomon E. Lifton of the Air Force will discuss "Disaster Control in Case of Atomic War," and Col. Don Flickinger "Space Medicine—Human Factor in High Performance Aircraft." On Friday, among others, Brig. Gen. Isador S. Ravdin will discuss plasma expanders, and Lieut. Col. Mathew Stockson "The Army's Role Under the Doctor's Draft." Dr. Morris Fishbein of Chicago is scheduled to speak. There will be entertainment, scientific exhibits, a demonstration of the ejector seat for aviators, and the helicopter ambulance rescue and evacuation. The program has been approved to give retirement point credit to reserve personnel who are not on the inactive list. Room reservations will be made for those desiring them. Correspondence should be addressed to the District Medical Officer, Building no. 1, Great Lakes, Ill.

ATOMIC ENERGY COMMISSION

New Policy on Use of Lie Detector.—The Atomic Energy Commission has established a new and restricted policy on the use of the polygraph, or lie detector, as a tool in its security program. Under the new policy, the present use of the lie detector at Oak Ridge, where it has been employed in periodic examinations of several thousand employees in security-sensitive portions of the manufacturing plants and the commission offices, will be stopped. At the same time, the commission has provided for the use of the lie detector in specific cases of security interest at any AEC installation but on a voluntary basis and on specific authorization, case by case, by the general manager.

The lie detector has been used in the atomic energy program only at Oak Ridge, where it was employed under the Manhattan Engineer District in 1946, and continued under the AEC management since 1947. On the basis of study of the use of the lie detector at Oak Ridge and in other federal agencies, the AEC has concluded that the machine's techniques offer only indeterminate marginal increase in security beyond that afforded by established and extensive AEC security measures and procedures. It was also concluded by the commission that the substantial cost of the Oak Ridge lie detector program in dollars, plus the intangible cost in employee morale, personnel recruitment, and labor relations, that might accrue from use of the machine substantially outweighed the limited advantage of its use. The study showed there is little data available indicating that the machine has any value in detection of intent to commit sabotage or espionage, or sympathy with subversive movements or idealogies. Its principal value was found to be in detection of pilferage.

PUBLIC HEALTH SERVICE

Training in Diabetes Control.—The Public Health Service announces that six courses for training in diabetes control will be held at the Diabetes Study and Training Center, Boston. The week-long courses will consist of discussions, demonstrations, and field trips. At present only two of the courses have been scheduled; they are (1) a diabetes program in public health (June 8-12, Sept. 21-25), planned for all categories of public health workers involved in the planning and operation of diabetes public health programs, and (2) group teaching of patients (May 25-29, Oct. 5-12, Nov. 30 to Dec. 4), planned primarily for personnel concerned with organizing and conducting group classes for patients with diabetes and their families. Enrollment will be limited to 10 per course. No tuition fee is required. Information may be obtained from the Diabetes Study and Training Center, 639 Huntington Ave., Boston 15, Mass. Applications must be received one month in advance of date of course.

FOREIGN LETTERS

BRAZIL

Microscopic Changes During Measles Eruption.—Dr. C. Magarinos Torres, head of the division of pathology of the Rio de Janeiro Oswaldo Cruz Institute, recently published a report on the microscopic changes occurring during a measles eruption. In an introductory note, he reviews the medical literature concerning the pathology of measles. Besides the skin lesions, he points out that others have been reported in the lungs, lymph nodes, spleen, bone marrow, liver, and adrenals. Lately, the most important feature reported in the measles pathology is the multinucleated giant cells found in the digestive tract, tonsils, spleen, thymus, and intra-abdominal lymph nodes, now known in the literature under the name of Warthin-Finkeldey giant cells. Dr. Torres emphasizes that there is no general agreement yet in the opinion of the authors about the nature of the cutaneous lesions observed during the eruption of measles.

The present study, based on material collected by the late Dr. J. de Castro Teixeira from 10 patients of the Evandro Chagas and the São Francisco de Assis hospitals, led Dr. Torres to the conclusion that the initial lesion of measles seems to be a hyalin necrosis of the epidermal cells, either isolated or in small groups; however, the association of epidermal lesions to alterations of the derma is an early occurrence, being reported as soon as 12 hours after the onset of the eruption. As a rule, during the period of time between the 13th and 36th hours, it is possible to find, in the same skin fragment, lesions in different stages of evolution intimately associated and consisting of small vesicles in the course of evolution to vesicopustules, which ultimately reach desiccation and desquamation. The author seems to be able now to consider as a pathognomonic characteristic of the measles eruption the presence of parakeratotic cells with intranuclear acidophilic inclusions as tentatively described by him and Castro Teixeira in 1932. He confirms the already known lesions of the derma consisting of edema of the papillae and infiltration of the pars papillaris and pars reticularis by great mononuclear cells, some of them containing numerous irregular granules intensely stained (Mallory-Medlar-Lipschütz). But his opinion is that these cells are macrophages that have ingested granules of keratohyalin as a consequence of changes in the process of cornification caused by the virus. The formation of vesicles and pustules, the study of which needs microscopic examination, characterizes the measles eruption. This characteristic leads one to put measles, an illness generally included in the exanthematic diseases, closer to the group of the pustular diseases, as herpes, chickenpox, vaccinia, and alastrium. Epidermal lesions were not found 72 hours after the outset of the eruption, while the dermal alterations did persist under the form of well-defined perivascular cuffs associated with moderate proliferation of fibrocytes.

Bengtson's Reaction Applied to the Diagnosis of Benign Rickettsioses.—In 1948, Dr. Plinio M. Rodrigues of the Adolpho Lutz Institute and Dr. J. Travassos of the Butantan Institute published a paper in which they described a human case of murine typhus that occurred in the city of São Paulo. The diagnosis was made by the isolation and identification of a strain of Rickettsia typhi. For a time, similar cases of mild infection observed in the state of São Paulo were not distinguished from cases of the so-called São Paulo typhus. They were later diagnosed as cases of murine typhus although only on clinical grounds. Further work was done by the same authors to clear up the etiology of such cases. Complement fixation tests with rickettsial antigens were carried out with a number of positive Weil-Felix serums. Many of the blood samples were taken, during or after the course of a mild infection, from persons living in either urban or rural areas of the state of São Paulo. At first a coctoantigen was used prepared from a strain of R. typhi isolated in Santiago, Chile. Later, Bengtson antigens were employed, prepared with Rocky Mountain spotted fever, murine, or epidemic typhus rickettsias. In 1944, serums from seven patients reported on in a rural area of São Paulo State were tested with coctoantigen. At that time, the lack of a Rocky Mountain spotted fever antigen made it impossible to prove conclusively the occurrence of cases of an exanthematic disease of the typhus group in the state of São Paulo. Two years later, complement fixation tests performed with Bengtson antigens permitted definite evidence that some of the so-called São Paulo typhus cases actually were cases of an infection of the typhus group.

Of the clinical cases tested with Bengtson antigens for complement fixing antibodies, 58 were selected for discussion in a recently published paper by the same authors. They were all mild cases with positive Weil-Felix reactions. In two of them, a serologic diagnosis of spotted fever was established. A positive test with either the murine or the epidemic antigen was obtained in 51 cases. In many of them there was not a significant difference between the murine and the epidemic antibody titers. Sometimes the titer was higher with the murine and sometimes with the epidemic antigen. From one of those 51 cases, a strain of R. typhi was isolated and identified. Serums of 75 employees of the grain store where this patient worked were tested with the Bengtson antigens. A positive test with the murine antigen was obtained from three of these serums. None of the persons had shown any sign of infection for a period of at least a month before the bleeding for the test. The test was also used for the diagnosis of four cases of laboratory infection accidentally contracted at the Rickettsial Diseases Laboratory of the Butantan Institute, where the work here reported was done. Complement fixation antibodies against the rickettsias of the typhus group were found in the serum of all patients when tested with the Bengtson antigens. Later, a strain of R. typhi was isolated from each case and identified. In one of these accidental cases, not even when using the Plotz antigens could a specific serologic diagnosis be made. A blood sample taken four months after the infection from this case was tested for complement fixation antibodies at the Army Medical Center, Washington, D. C. The titer was slightly higher with the epidemic than with the endemic infection antigen; however, the agglutination titer with the murine typhus was higher than with the epidemic rickettsias.

Peritoneal Flooding Caused by Uterine Perforation from Choriocarcinoma.—Drs. Martiniano Fernandes and Moraes Neto of the Encruzilhada Maternity Hospital, Recife, state of Pernambuco, described recently two case histories of peritoneal flooding caused by uterine perforation in consequence of choriocarcinoma. Between the extremes of being considered the most malignant of all the genital tumors (Mathieu) and the opposite of presenting the possibility of spontaneous cure in 10% of the cases (Novak), the choriocarcinoma may present, during the course of its evolution, dramatic accidents of sudden appearance, which make the prognosis still more unfavorable. One of these grave occurrences is the uterine perforation causing peritoneal flooding, as in the cases of Fernandes and Moraes Neto of Recife. They reviewed the medical literature of the last 20 years, finding a total of 46 similar cases, a number that they certainly evaluate incorrectly, since many such cases were not published as a consequence of lack of diagnosis, and several others, reported under that title, may have been of certain types of dissecting moles inadvertently classified as choriocarcinoma. The authors reach the conclusion that only in cases with special antecedents associated with facts picked up during a particularly favorable clinical examination is it possible to make a correct diagnosis, before operation, not only of the accident but also of its choriocarcinomatous origin. Regarding the prognosis, one easily realizes its great gravity, since when choriocarcinoma has already destroyed the uterine wall its evolution has reached the final stage, with little possibility of therapeutic success.

The items in these letters are contributed by regular correspondents in the various foreign countries.

ITALY

Annual Pediatric Meeting.—The Italian Society of Pediatrics held its annual meeting in Florence under the chairmanship of Prof. Cesare Cocchi, director of the pediatric clinic of the university of that city. Numerous Italian and foreign pediatricians and many surgeons were present.

The medical part of the first report, hydrocephalus in infancy, was discussed by Professor Bentivoglio, director of the University of Padua pediatric clinic, and by his co-workers Professors Bolletti and Sartori; Professor Visalli from the University of Rome discussed the surgical part. Professor Bentivoglio discussed some fundamental points. Hydrocephalus is usually classified as active or passive. The latter represents only the epiphenomenon of morbid or abnormally-formed processes of other origin and never becomes a well-differentiated clinical entity. Active hydrocephalus should be considered the expression of an imbalance between production and reabsorption of the cerebrospinal fluid and has greater clinical importance than the passive type.

There are two possibilities for the pathogenesis of these forms: Either excess production of cerebrospinal fluid is not compensated for by increased reabsorption or there is an obstacle to its reabsorption at some point in the pathway along which the fluid travels from its place of production to its place of reabsorption. According to Professor Bentivoglio, only one form of hydrocephalus attributable to the first possibility has already been proved, and this is hydrocephalus due to adenomas of the choroid plexuses. All the other forms of hydrocephalus due to hypersecretion, according to him, have not been definitely proved to exist. In fact, often it is not possible to demonstrate obstruction in the fluid bed and especially the leptomeningeal cortical spaces. In these spaces there may be obstacles that, caused by inflammatory processes or their results, block the terminal reabsorption of the fluid. Since, however, it is difficult to demonstrate their presence and there are no other obstacles in other parts of the pathway, many times the hypothesis of hydrocephalus due to hypersecretion becomes very uncertain.

Professor Bolletti discussed the pathogenesis of hydrocephalus in infancy. Hydrocephalus caused by a defect of drainage, he classified into three types: The first consists of the commonest forms of hydrocephalus attributable to obstructions in the pathways of drainage, which may result from congenital malformations, neuromeningeal inflammatory processes, expanding processes within the cranium, intracranial hemorrhage, and trauma to the cranium. The other two types are secondary to lesions of the last points of the fluid exit or to deviation of the fluid in the subdural area because of lesions to the arachnoid. An *ex vacuo* hydrocephalus in infancy is most commonly caused by cranial trauma.

Professor Sartori discussed the subject from the clinical point of view and reviewed the symptoms that help to establish the diagnosis. Often an active hydrocephalus begins as a condition merely symptomatic of other processes, but it later assumes a clinical autonomy in which sometimes the initial pathogenetic mechanisms are associated. The symptomatology and the course of the syndrome depend greatly on the age of the patient at the time of onset of the disease. The speaker reported on the unusual symptomatology of hydrocephalus and the phenomena that can be perceived by percussion of the brain, auscultation, transillumination, and puncturing of the fluid spaces. Pneumoencephalography and cisternography are the latest methods of investigation that help to determine exactly the diagnosis.

Professor Sartori said that the medical treatment of fully developed active hydrocephalus is substantially palliative and except for a few exceptions there are no worthy and convincing proofs of its real efficacy. Among the elements of medical therapy are puncture into the spinal canal to reduce the pressure, administration of potassium iodide, and intravenous injections of hypertonic magnesium sulfate or glucose solutions.

Professor Visalli reported on surgical treatment of hydrocephalus. The operation may aim to diminish the fluid secretion, or to deviate the fluid toward points of reabsorption other than the physiological ones or toward the exterior. Another method of treatment may be the removal of the obstructing cause or the creation of new pathways of fluid communication, with exclusion of the obstructed section. The speaker concluded that the results that have been obtained are not satisfactory, but he believes that the failures are mostly attributable to a late intervention.

Professors Pagani-Cesa and Ortolani reported on the social aspect of medical help to the child after he returns home from the hospital.

Fasting as Means of Investigation.—At a meeting of the Medical and Surgical Society of Pavia, Professors Gastaldi and Fedeli read two papers on the fasting test used to investigate the metabolic processes. The first paper was on the value of fasting in patients with liver disease. This varies greatly according to the type of disease and to its gravity. The most characteristic changes were seen in patients with catarrhal jaundice, in whom, when the liver parenchyma was altered, there was no relationship between the stimulation of the organs of endocrine regulation, especially the adrenal gland, and the metabolic response represented by increased elimination of urea. In fact, the speakers observed in their patients a low elimination of urea, which changes slightly with reference to the carbohydrate necessities. As a consequence of this behavior in some cases glycemia falls below the normal values. In general the ketonic bodies are decreased, but there are cases in which an increased ketonemia may be observed and it may be interpreted as an increased catabolism of lipids.

The second paper was on the fasting test used to investigate the metabolic processes in patients with diabetes mellitus. The speakers studied the behavior of glycemia, ketonemia, and elimination of urea and ketones in patients in whom the disease was of average gravity. They found that glycemia is notably decreased during the first 12 hours of fasting; when it has reached the minimum hypoglycemic value it can remain stationary at this value or else it can increase moderately during the final phase of the test. The decrease in glycemia is not in direct relationship with the catabolism of proteins, which can be estimated by studying the elimination of urea. During the fast this may be within values above the normal or clearly below. Ketonemia that is moderate or of average entity at the beginning of the test does not increase much during the second 12 hours. Elimination of ketone bodies with the urine, which is generally moderate, does not undergo pronounced increases with the increasing of ketonemia. The behavior of urea elimination and of ketonemia in diabetic persons is related to a particular ratio in that patients with high elimination of urea have low ketonemia and vice versa. On the basis of these experimental data the speakers advanced some considerations on the correlation that exists in diabetics in the metabolism of the principal energetic sources during a prolonged fast, and they emphasized the relative independence of the behavior of glycemia in comparison with the catabolism of proteins and lipids. According to the speakers, ketonemia has importance as an index of the activity of the processes of lipid catabolism; in some patients it is possible to find evidence of an adrenal hypofunction by the fasting test.

Professor Gastaldi reported on elimination of ketone bodies during the fasting test. He observed that the elimination of ketone bodies with the urine is not in direct relationship with the behavior of ketonemia. On the contrary, this is linked with the behavior of all three metabolisms since pronounced ketonemia appears with symptoms that indicate a pronounced utilization of the energy-producing material from carbohydrates and proteins.

Vertebral Osteomyelitis.—At a meeting of the Ionic Society of Medicine and Surgery Professor Buonsanti read a paper on the common features of various forms of vertebral osteomyelitis. He showed that in the vertebra inflammation is localized in the spongy structure, which has the necessary pabulum for the infection. This is contrary to the belief of those who attribute to the neural arch a role that it assumes only in exceptional cases. In discussing the degeneration of the intervertebral disk and Schmorl's nodules within the spongy tissue, the speaker, on the basis of Schmorl's own monograph, showed

the various foreign countries.

stage, with little possibility of therapeutic success.

that this roentgenographic and anatomicopathological change takes place through an inclusion of fragments of the disk that were sent into the spongy substance of the soma after this slipped because of the primary osteomyelitic focus.

Professor Buonsanti agrees with Charmandaryant and Sorrel that roentgenograms are of no help in cases in which the somatic process is central and limited in extension. He believes that all vertebral osteopathies—pyogenic, coccigenic, and syphilitic—independently of the various etiological hypotheses, may be reduced to the two parabolic phases of halisteresis and sclerosis. The first of these phases is destructive, and the second is reconstructive and is often interpreted as a direct expression of the bacteria. Professor Buonsanti said that the favorite localization of osteomyelitis is the dorsolumbar part; this is due to the particular mobility and the particular volume of the soma, which in this point obeys the laws of growth described by Murk-Jansen.

LONDON

General Practitioners in the Health Service.—The Minister of Health, Mr. Iain Macleod, discussed the status of general practitioners in a series of three recent speeches, which represent the official view and portend any likely changes that may happen in the near future. He referred to some of the questions that demand an early answer, such as whether the demands on hospitals can be reduced without detriment to the patient, whether general practice is as well organized as it might be, and whether hospitals provide sufficiently for general practitioners. These questions concerned the medical profession, the administrative machine of the service, the executive councils and their partners, the hospitals and local authorities, as well as other professions in the service. The result was that many persons became concerned about the future of general practice within the framework of the National Health Service.

Mr. Macleod said that the following trends should be encouraged: 1. Full cooperation between general practitioners and the local authorities' domiciliary services would relieve pressure on hospitals for beds. 2. There should be an increase in the number of partnerships and the development of practice by groups of physicians working together as teams. 3. A better distribution of physicians would avoid overloads of patients. 4. Closer association between family physicians and hospitals would encourage contact between the physicians and their patients in hospital and provide direct access to roentgenographic and pathological departments. 5. The family physician should become the leader of a team comprising all the services provided by the local health authority according to the needs of the patient. 6. There should develop closer cooperation among physicians, dentists, opticians, and chemists working under the executive councils. "With all the recent advances on the scientific side of medicine, hospital treatment has become so elaborate and so expensive that it is imperative to reserve it for patients who really need it and can benefit by it," said Mr. Macleod. "Patients ought not to be sent into hospital unless they need an investigation or other treatment which can only be given to them as inpatients, or their homes or other social circumstances make it essential for them to be admitted where purely medical needs may not." If these principles were maintained, the clinical interest of general practitioners' work would be greatly increased. "If patients are sent to hospital only when necessary and discharged as soon as their condition permits, a very great inroad could be made on the waiting lists which for some conditions could probably be made to disappear. Moreover, it would often be of positive benefit to the patient. Many patients—particularly old people and children, who fret when away from home—are far better at home in the care of their own doctors or receiving treatment from hospital as outpatients backed by all the ancillary domiciliary services. Home conditions must, of course, be suitable for home-care, and bad housing and overcrowding will unhappily still take time to eliminate, despite the immense concentration of effort being applied to solving the housing problem."

New forms of group practice should also be evolving in the recently opened experimental health centers. Under the Danckwerts award, total remuneration would keep pace with the number of physicians. When a good distribution had been secured, the Ministry and the profession would have to agree as to the proper rate of entry into general practice, and arrangements would have to be made to link remuneration to that rate. "The Exchequer," said Mr. Macleod, "clearly cannot finance an unlimited increase in the number of doctors beyond the point at which the best practicable distribution can be secured consistent with the proportion of the national resources that can be devoted to this purpose." Mr. Macleod was of the opinion that patients would receive better care, equipment, and premises, although one had to admit that from the angle of the patients some facilities were quite inadequate. "I am sure the profession will be the first to wish to put this right," he said. "Group practice should also benefit the doctor, who should have easier access to colleagues' opinions, better equipment and premises and a more reasonable life, with better provisions for time-off and holidays."

General practitioners in small towns and rural areas (and some others), in his opinion, should be able to have charge of their own patients who do not need specialist care but need admission to hospital, and selected general practitioners should hold specific posts of various kinds part time. These posts might be of a general character; for example, they might act as medical officers of a convalescent home or take the place of residents or registrars, or they might take posts of a specialist character where they can act as assistants to consultants. These specialist posts might provide an opportunity for a general practitioner to become a specialist himself.

General Medical Services Committee.—National Health Service physicians are pressing for modification of the disciplinary machinery used against them when they are alleged to have broken their terms of service. They have proposed more than 20 amendments to the Ministry of Health. Aim of the proposals is to limit the present "autocratic powers of the ministry." There is much criticism of the length of time, sometimes more than a year, cases are allowed to drag on. The amendments have been approved unanimously by the committee. This committee negotiates on behalf of the 20,000 family physicians in the service.

The physicians have also endorsed the policy that they should be entitled to complain of patients who make frivolous and unreasonable demands on their services. This right, with fines for patients found guilty, existed under the old national health scheme. A British Medical Association spokesman said: "We want that provision restored. We want the Ministry to draw up a code of behaviour for patients." The committee decided against asking for a right of appeal to the courts for physicians found guilty. Instead, they recommend that the person appointed to hear an appeal should be a practicing barrister or solicitor of at least 10 years' standing, appointed by the Lord Chancellor. The committee proposed that the time limit for making complaints against physicians should be four weeks. At present six weeks are allowed.

Among the matters discussed was the question of delay in dealing with charges of excessive prescribing. A case from the North of England was mentioned in which an allegation was made against the practitioner in August, 1951, the hearing before the committee took place in December, the hearing of the appeal in August, 1952, and yet no decision had been announced by the end of October. Another case mentioned by a member had dragged on for nine months. It was agreed that the matter should be taken up with the Ministry.

Hospitals' New Economy Rule.—Hospitals must, in the future, apply to the Ministry of Health for permission to employ extra physicians or nurses. This is the latest measure taken by Mr. Macleod, Minister of Health, to ensure that hospitals are staffed economically. In a memorandum to regional hospital boards and other authorities he asks for a 5% cut in non-medical staffs in the coming year. Liftmen, gardeners, and maintenance men are included.

NORWAY

Norwegian Field Hospital in Korea.—In a report on the Norwegian field hospital in Korea staffed by 14 physicians, 14 nurses, and 5 orderlies, Dr. Arne Hvoslef points out that it was originally planned as a 60-bed hospital but that by an extension many more than 60 patients could be accommodated. Up to October, 1951, there was a fairly steady routine, with admissions ranging between 100 and 200 per week. Later on, when the hospital was moved closer to the front, the pressure of work became more urgent. Between July 18, 1951, and May 15, 1952, there were more than 6,000 admissions, including 2,500 Americans, more than 2,700 patients from the United Kingdom, 600 civilian Koreans, and 180 prisoners of war, mostly Chinese. In the same period operations numbered 2,205, and the highest rate was 150 operations per week. Valuable advice on treatment was given by the U. S. War Department, and every week circulars were distributed with information about surgical problems.

Though in principle the patients were sent on to base hospitals as soon as possible, those who had undergone laparotomy were found to stand transport so poorly that they were kept at the field hospital for 9 to 10 days whenever possible. There was no shortage of transfusion blood, which was flown from the U. S. and which was supposed to be used within the first eight days after delivery. But this interval was often doubled with impunity, and the Koreans given blood three weeks after its delivery tolerated it well. To avoid its being shaken for three or four hours during mobile transportation, blood was often transported by helicopter. Little use was made of plasma and serum, and none was made of dextran and similar preparations. All the wounded were given penicillin and antitetanus preparations on admission to the hospital. U.N. patients already vaccinated against tetanus received only toxoid, whereas Korean and Chinese patients were given antitetanus serum. Dr. Hvoslef, whose report is published in the organ of the Norwegian Medical Association, *Tidsskrift for den norske laegeforening*, is not in favor of the tourniquet, which was usually found to be unnecessary, faultily applied, and causing harm.

Laboratory Tests in Hospital.—Dr. Trygve Braatöy, who has recently resigned his appointment as head of the psychiatric department of Ullevaal Hospital, spoke bluntly on the subject of hospital maladministration at a meeting of the Norwegian Medical Society on Sept. 10. In his opinion, a superfluity of laboratory and other tests is at present seriously interfering with any effective contact between patient and physician. On the medical side he has perused the records of 100 patients in Ullevaal Hospital who, in the period 1916-1918, underwent a total of 231 laboratory tests. In the same hospital during the period 1946-1948, the records of 100 patients showed that they had undergone 1,311 laboratory tests, an increase of 470% of such tests in 30 years. In the same two periods, Dr. Braatöy found that, in the first period, the case records of 30 patients admitted for the first time weighed 740 gm. altogether, whereas, in the second period, the weight of the same number of case records had risen to 3,500 gm.; the weight of the paper work by the authors of these records had increased about 370% in the course of 30 years.

Dr. Braatöy recalled the time, more than 20 years ago, when as a psychiatric intern he was doomed to the drudgery of performing laboratory tests of no particular clinical importance to patients with whom he came into comparatively little clinical contact. Wholesale Wassermann tests of 65 persons showed negative reactions in 95%, and it was evident that much of this testing was undertaken at random, not because there was any special indication for it. Dr. Braatöy concluded that if the present tendency to carry out unnecessary tests is allowed to continue in a spirit of automatic routine, then teaching hospitals are bound to suffer financially and intellectually.

Centralization of Harelip Operations.—A recent editorial in the organ of the Norwegian Medical Association, *Tidsskrift for den norske laegeforening*, draws attention to the problems, solved or still awaiting solution, concerned with cleft palate and harelip. The scope of these problems can be roughly gaged by the calculation that some 65,000 babies are born yearly in Norway and that 1.5 per thousand of them are born with these disabilities. This means that at least 100 such cases arise every year. Unfortunately they need not be recorded at birth, and accurate data on the subject are therefore not yet available. Uniformity of operative procedure is also still lacking, and in the past it has been customary to recommend a plastic operation for harelip at the age of 6 months and closure of a cleft palate at the age of 2 years. Elsewhere these operations are undertaken at a considerably earlier age, and in the latest edition of a Scandinavian textbook of children's diseases, Siwe recommends a harelip operation as soon after birth as possible and closure of a cleft palate at the age of 12 to 18 months.

In Norway there is no lack of surgical talent, but its organization and distribution are still imperfect. In principle it is easy to agree over the desirability of these operations confined to surgeons in a position to specialize in plastic surgery, with ample material on which to work. Every large town should have its own specialist working in a central hospital that caters to this town and neighboring districts. In Oslo, for example, such a specialist service has been provided at the Rikshospital, where the available accommodation for these cases has hitherto proved so inadequate that beds have had to be sought in other hospitals in the city. Because these hospitals are private, the cost of treatment has proved relatively high, and the aim of centralization has, to a certain extent, been defeated on this score. Meanwhile, the other large towns in Norway do not enjoy even the partial centralization provided in Oslo, and plans have still to be worked out not only for the operative treatment of these cases but also for their prolonged postoperative care in the charge of a team consisting of dentists, nurses, and specialists in phonetics and diseases of the ear, nose, and throat. The medical profession is urged to cooperate in forming a centralized institution charged with keeping a record of all these cases and ascertaining the necessary requirements for beds in suitable localities.

Long-Acting ACTH from Whale Pituitary.—A preliminary note has already appeared in these columns (*J. A. M. A.* **150:**151 [Sept. 13] 1952) on the work of Dr. O. Römcke and Dr. J. H. Solem at a hospital in Drammen where they have given a Norwegian long-acting corticotropin preparation, "cortico-depot," with very promising results. "Cortico-depot" (Nyco) is a suspension of a corticotropin-zinc-protamine complex in an aqueous phosphate buffer. The sterile suspension is characterized by high suspensibility and low solubility. The source of this preparation is the anterior lobe of the whale's pituitary.

At a meeting of the Trondheim Medical Society on Oct. 22, 1952, Dr. Solem gave an account of the observations that he and Dr. Römcke have made of 30 patients treated continuously with "cortico-depot" for an average of seven months. In addition to 20 cases of chronic rheumatoid arthritis, there were 2 of Bechterew's disease, 5 of chronic asthma, 2 of scleroderma, and 1 of pemphigus vulgaris. An intramuscular injection of 20 I.U. of "cortico-depot" was given every second to third day and was found to be the smallest dose consistent with satisfactory but not complete control of the symptoms. The dosage was small enough to avoid significant side-effects. Dr. Römcke and Dr. Solem have dropped the classic schedule for long-term treatment with corticotropin, high suppressive doses at the start followed by gradual reduction to a lower maintenance dose. In the long run, an initial and complete control of the symptoms could not be maintained by doses small enough to avoid distressing side-effects. Because of this experience, Dr. Römcke and Dr. Solem have, from the very start, given the small maintenance dose and have found this to be a far more satisfactory procedure. In five patients resistance to whale "cortico-depot" developed, and it would seem that increased tissue inactivation played an important part in this phenomenon, as all the patients responded well to whale corticotropin given by intravenous injection. A trial with different corticotropin preparations from pigs showed that these patients had also become refractory to intramuscular injections of pork corticotropin of the same potency; however, all of them had a very satisfactory adrenal response with a pork "cortico-depot" made from a corticotropin purified to a 10 times greater specific activity. The solution of the phenomenon of development of a refractory state to corticotropin given by intramuscular injection may, according to the observations of these doctors, be closely related to the problem of introducing high-potency, purified corticotropin preparations for therapeutic use.

applied to solving the housing problem."

maintenance men are included.

SPAIN

Congress of Pediatrics.—The Eighth National Congress of Pediatrics was recently held in Barcelona, with Dr. J. A. Alonso Muñoyerro of Madrid presiding as president. The congress decided to "respectfully request" the authorities concerned to help resolve the social problems involved in the crusade against tuberculosis in Spain. The most pressing needs include the creation of antituberculous centers, and the distribution of certain drugs by the Department Seguro Obligatorio de Enfermedad. Because the incidence of endemic infantile kala-azar is great in Spain, the following measures should be established: obligatory reporting of cases of the disease; distribution, in rural areas, of pamphlets showing the symptoms of the disease; and generous distribution of the most reliable preparations for the treatment and cure of this disease; for the better knowledge of the health of children, the study of growth has an extraordinary national interest as a source of data on which standards of growth in normal children in Spain could be based. Uniform criteria in the selection of measurements to be made and in the technique used should be established.

In acute forms of infantile tuberculosis, the isoniazid compounds are of extraordinary value. The treatment should be given under supervision of a physician, and the drug should be given concurrently with antibiotics. Vitamin deficiencies appearing in the course of treatment should be controlled by adequate vitamin therapy. Laymen should be informed of the specific contraindications to the use of antibiotics and of the effects of improper use of these substances.

The Eighth Congress on Pediatrics advocated intensification of BCG vaccination in children in both rural and urban areas. Vaccination should be given individually or en masse. Steps should be taken to obtain soon passage of a law requiring BCG vaccination. The congress also noted the need for a law governing medical requirements for teachers, both of religious orders and secular, as they are in close contact with the pupils. The previous conclusion of the Congress of Pediatrics that the need is urgent of extending the requirement of a medical examination of teachers to the whole country aims to give protection to all children. Laws are needed requiring that the work of children end when the hours of school are over, and prohibiting teachers from giving children homework to be done in extraordinary hours.

To complete the program to decrease infantile mortality, the congress advises establishment of clinics for infants, especially for premature infants and for infants who are congenitally weak. Legislators and sociologists are requested to find a way whereby natural parents who abandon their children would lose their rights of *patria-potestas* on the children and that the latter should be adopted by honorable families.

Program Honoring Ramón y Cajal.—A medical week was held in the Faculty of Medicine of the University of Madrid, Nov. 14-20, in celebration of the centenary of the birth of the famous Spanish histologist, S. Ramón y Cajal. The sessions were held in the same rooms in which Ramón y Cajal gave his lectures to his pupils, and were attended by scientists of Spain and foreign countries. It was officially inaugurated by Dr. Lain Entralgo, the rector of the University of Madrid. Dr. Lain Entralgo had the place of honor among the following physicians: García Orcoyen, dean of the Faculty of Medicine, Enriquez de Salamanca, professor of medical pathology, Sanz Ibáñez, the director of the Instituto Cajal, Jiménez Díaz, professor of medical pathology, and Fernando de Castro, professor of histology. Prof. Jiménez Díaz spoke in memory of Ramon y Cajal. The audience heard a phonographic record of a lecture delivered by Ramon y Cajal, and many articles were read honoring him.

Scientists attending the celebrations were entertained with receptions in the Municipal Hall of Madrid and in the Instituto de Cultura Hispánica, a visit to Toledo, an amateur bull-fight in the Castillo de Higares, which was a property of Columbus, a trip to the Royal Monastery El Escorial, a banquet given by the general directors of the department of cultural relations of the Ministry of the Exterior, and a gala banquet in the Casino de Madrid.

TURKEY

Centenary of School for Midwives.—A ceremony was held at the Istanbul Municipal Haseki Hospital in honor of the founding of the first school for midwives in 1852. Presentation of diplomas to this year's graduates took place in the presence of the city's honoraries, the professors of the universities obstetric departments, their assistants, and medical students. In 1919 the American Hospital in Istanbul opened a training school for nurses, and a year later the Turkish Red Crescent Society established the first school for nurses at Istanbul-Haydarpacha and then Istanbul Aksaray. Hitherto nursing in municipal, military, and other hospitals was done by practical nurses and male nurses, who, at the most, had had a short course in practical nursing. Trained midwives were often in charge of hospital wards.

The Ministry of Health and Social Assistance has two training schools for nurses in Istanbul and one in Ankara; the establishment of four more such schools in other parts of Anatolia is under consideration. Applicants for the school for midwives must be between 18 to 25 years of age and must have had five years of grade school and three years of junior high school training. The theoretical and practical instruction takes two years and is followed by six months' practical experience in a maternity hospital. Board, maintenance, and tuition are free. Theoretical instruction is given by professors from Istanbul University. The students study at the expense of the Ministry of Health and must work for a period of five years after termination of the course. If they terminate their work before that time they are obliged to repay the expenses incurred in their training in proportion to the time served. Currently there are more than 2,000 trained midwives in Turkey. Every township municipality employs at least one. The midwives receive a salary but get no fees for attendance. The municipality supplies the bag with instruments and other medical supplies. If there are complications a physician is called or the patient is sent to a maternity or nearby hospital.

In 1940 the Ministry of Health opened two schools for village midwives, one in Konya and one in Balikesir. These courses take one year and are followed by six months' practical experience in a maternity hospital. The graduates of these schools attend to births only in villages. They are in the employ of the Ministry of Health and receive a salary from the ministry. They are not permitted to practice in other but rural communities and are also under obligation to work for a period of five years or repay the ministry for expenses incurred in their training. The ministry supplies the kit bag and instruments. The number of these midwives is steadily increasing. There are almost 1,000 engaged in almost all 63 provinces and 40,000 villages, with a resultant downward trend in maternal and child mortality. The first modern medical school in Turkey was established under Sultan Mahmoud II in 1827 in Istanbul at the Pera-Galatasaray. Until that time medical education had been of the scholastic type. The first school of veterinary medicine was established in 1839.

Eight Digits on One Hand.—Dr. Asil Mukbil Atakam, chief of the surgical department of the Istanbul-Pera Municipal Hospital, reported that a middle-aged woman with eight fingers on the left hand was accidentally discovered among the dispensary patients. The condition is congenital. Radiological examination revealed atrophy at the distal end of the radius; the distal end of the ulna is divided in two; the styloid process is absent; instead of 8 ossa carpi there are 12; in place of 5 metacarpals there are 8; and the thumb is replaced by 4 metacarpals. The first four metacarpals are ¼ in. apart from the second four. The terminal phalanx of the fourth digit consists of several small bones; the first phalanx of the fifth digit is slightly curved; and the other digits are normal. The patient's right hand is normal as are also the movements of the left hand, and the four extra digits do not encumber the patient as they perform the function of the thumb. There is no heredity evidence, no syphilis, and no abnormality in the patient's children.

disabilities. This means that at least 100 such cases arise every

for therapeutic use.

CORRESPONDENCE

MISNOMERS IN MEDICAL LITERATURE

To the Editor:—Our great medical literature, of which every American physician may justly be proud, is unfortunately invaded and gradually deglamorized by the fifth column, by the crippling infiltration of injudicious use of phrases, terms, expressions, and even medical "slang," which could have a place only in a second rate farce or rather corrupted vulgar screen version of true medicine. Great works of great men of genius and science need great discretion and careful choice of terms and definitions used in scientific expressions.

The purpose of this letter is to point out at least several too common errors found in almost every nationally known and highly esteemed medical magazine and to suggest to the American Medical Association the formation of a committee with the definite purpose of eradicating such errors (e. g., by issuing an authoritative booklet with an explanation of such errors and accumulating such information for the use of all physicians, possibly with revisions, as medical terms and ideas may change with ever-growing progress and new discoveries). In view of the fact that more detailed enumeration of misnomers would easily take a solid volume and since I am not allowed more space, I limit myself to several of the commoner misnomers.

1. "My patient has an 'acute appendix.' " For well over two centuries the use of "itis" to describe an inflammatory condition has been postulated, and if inflammation is meant why not indicate it by the use of proper expression: "appendicitis."

2. Dr. X. writes an excellent article, which I wish more practitioners would read and learn, but he states: "His fasting blood sugar was 280 mg. per cent." Here again, please, remember that in estimation of the glucose level of the venous blood, milligrams per 100 cc. of blood are used, and to present a true picture in percentage it should be 0.28%, as milligrams must be converted to grams, which correspondingly are compared to 100 cc. To present milligrams in proportion to cubic centimeters is definitely wrong and confusing, as every properly qualified specialist in this field knows or should know.

3. An attending physician writes on the chart requesting that the intern inject intravenously 500 cc. of "normal saline." What he really means or must mean and definitely must understand is that it should be 0.9% sodium chloride solution in distilled water, i. e., isotonic or physiological solution of sodium chloride, which keeps blood elements in natural suspension, since both hypertonic and hypotonic solutions would be injurious to blood elements.

4. Reading one of the most important and internationally recognized of our medical magazines, I came across the statement: "Patient's urine contained heavy amorphous crystals sediment." Now, this is an entirely contradictory statement. If sediment was amorphous it was not supposed to have any shape, and how did it happen that it contained plenty of definitely formed crystalline bodies? And, even so, what kind of crystals were they? This is just one of numerous examples of inability to think clearly and inability to express clearly one's ideas.

5. But why take examples from magazines? Let us take a book, the textbook for medical students and doctors of medicine. In one of these I read: "The red corpuscles or erythrocytes are elastic, specific gravity 1088, non-nucleated, and average about 1/3,000 line in diameter." The book is excellent and is written by a respectable scientist. I do not doubt for a second the great knowledge and competence of the author, and nevertheless measurements in form of obsolete designations which were still proper in first three-quarters of the 19th century could not be informative in the 20th century, as now for clearness of presentation in scientific matters we must use the metric system. This is important in hematological diagnoses; e. g., in pernicious anemia (Addison-Biermer anemia) the size of the red cells has an important diagnostic significance. While in the peripheral blood of the normal adult erythrocytes are from 7 to 9 μ in diameter, in pernicious anemia macrocytes reaching 12 to 15 μ in their longest dimension are found. There is nothing easier than to estimate erythrocytic diameter in units of metric system, as above. Therefore, designation of erythrocytic measurements by fractions of thousandths of a line is now, in 20th century works, a misnomer and as such has to be excluded from scientific presentations of any kind as a confusing statement.

6. Let us look at the request slip for clinical laboratory work: "Doctor requested a 'metzhemoglobin' test on this patient." "Please, do a complete blood account on him." "I am sending these specimens for complete gastric urinalysis on the patient." The nurse from the clinic wants to know: "Which is the domineering organism?" (Why, do the bugs have dictators also?) "This is a specimen of uterine scratchings." Look for "sick cell anemia." "Rossini test for syphilis." "Kastelanetz" ointment (with apology to my dear old friend Aldo Castellani). Stool for "askult" blood. "Piece of large testine with momentum attached." By the very style of this report you can see who did it: "There were two pigeon egg's size gallstones found in this urinary bladder. . . ." I do not wish to sound dull and monotonous by recounting several hundreds of such "classical" expressions of ignorance, superficial knowledge, or complete neglect of English language.

I remain silent when they kill Latin; there is no use in fighting. Latin is already dead and cannot become "deader" (using their expression). But literary English is very much alive and even can claim recognition as a living international language joining at least temporarily many a nation and many a tongue. All our contemporary progress depends on clear thinking, clear understanding of the problems involved, clear and concise writing, and correct presentation from the standpoint of syntax, common sense, logic, and correct scientific background. Before concluding this letter, I wish to state that it has been written with malice toward none and its only purpose is to advance our medical literary consciousness.

In conclusion, I wish to emphasize a few points of importance. Having full evidence that many unscientific expressions, as a dreaded fifth column, have crept into serious and even classical medical literature, we must apply definite efforts to correct this unfortunate situation. If our medical literature is coming of age and begins to suffer degenerative changes with hardening of the arteries, we must rejuvenate it and purify through a permanent, authoritative committee of the A. M. A. While this proposed committee in accordance with our free democratic principles should not have any power to influence directly any writing, it should explain, correct, and clarify all doubtful medical terminology. This committee should serve as a court of last appeal in disputes arising as to the correct use of medical expressions and usage. This committee could issue from time to time authoritative explanations as to moot medical literary questions. We have Webster for general literature, but we must have our medical Webster.

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PHYSICIANS FOR CEJWIN CAMPS

To the Editor:—The Cejwin Camps, which are a nonprofit, tax exempt camp organization, now preparing for the 35th consecutive year of operation, at Port Jervis, N. Y., require physicians in the infirmaries for the boys' camps and the girls' camps. Each infirmary has a resident staff of two physicians and five nurses (including a night nurse) during the months of July and August. Physicians should be available for either July or August or for both months of the summer. The salary is $600 for two months or $300 for one month, plus full maintenance in each case. Family accommodations are available. Interested persons may obtain further information from me at the address below.

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THE "BLIND PLACEBO" IN THE EVALUATION OF DRUGS

To the Editor:—In recent years a number of investigators have emphasized the importance of placebo controls in the accurate evaluation of drugs (Hill, A. B.: *Brit. M. Bull.* **7**:278, 1951; Marshall, E. K., Jr., and Merrell, M.: *Bull. Johns Hopkins Hosp.* **85**:221, 1949; Conferences on Therapy: *New York State J. Med.* **46**:1718, 1946; Ross, O. B., Jr.: *J. A. M. A.* **145**:72 [Jan. 13] 1951; Beecher, H. K.: *Science* **116**:157, 1952; Wolf, S.: *J. Clin. Investigation* **29**:100, 1950; and Todd, J. W.: *Lancet* **2**:438, 1951). In spite of these reports, and in spite of the elementary aspects of control groups in biological research, the majority of medical investigators continue to report observations and draw conclusions on drug efficacy based on uncontrolled studies. The purpose of this communication is to emphasize again the necessity of the control group in the clinical investigation of drugs and more specifically to point out the value of the "blind placebo"—"blind" to both the patient and the physician.

TABLE 1.—*Antihistaminic Drugs and Ascorbic Acid in Colds* *

	Placebo	Ascorbic Acid	Phenindamine Tartrate	Ascorbic Acid plus Phenindamine Tartrate	Tripelennamine Hydrochloride
Average duration of colds in previous years, days	13.0	12.2	11.5	10.8	13
Average duration of colds treated in this study, days	5.1	5.6	5.7	5.6	5.2

* Adapted from Cowan and Diehl (J. A. M. A. **143**: 421 [June 3] 1950).

The term "blind placebo" as used here indicates that the investigator is supplied with both the experimental drug and an inert preparation (such as saline or lactose) so labeled that neither he nor the patient is aware of the identity of the medicament being administered. It might be argued by some that the use of the blind placebo is not ethical and is unfair to the patient, at least to those who are unlucky enough to fall into the placebo group. (In many instances, of course, the placebo group turns out to be the "lucky group.") This argument is not sound, since the purpose of a study is to determine whether the new drug is in fact actually beneficial in a given disease; hence, withholding a drug with questionable activity can hardly be consider unethical.

There are two main reasons why it is necessary to employ the blind placebo in the accurate evaluation of a given therapeutic agent: (1) to prevent the tendency of the investigator to overlook the natural course of a given disease and (2) to rule out psychological factors on the part of both physician and patient. Most of us tend to forget that many acute conditions are self-limited and that the patient will get well in spite of the therapy and not because of it. It must be remembered that most headaches, diarrheas, sore throats, and the like will disappear without any therapy. Just the fact that a drug is given and the patient improves is not proof that the drug caused the improvement. The evaluation of the treatment of chronic disease is even more difficult because of the usual clinical course of remissions and exacerbations and "good and bad days."

TABLE 2.—*Antihistaminic Drugs and Side-Effects* *

Symptom	Five 50-mg. PBZ † Tablets in 24 Hours (100 Trials)	Ten 50-mg. PBZ Tablets in 24 Hours (56 Trials)	Placebos, 5 in 24 Hours (102 Trials)
Drowsiness	37	48	30
Headache	26	36	42
Nausea	17	23	8
Dizziness	24	41	15
Nervousness	13	21	15
Dryness of mouth	29	45	30
Insomnia	12	23	6

* Adapted from Brown (Proc. Soc. Exper. Biol. & Med. **67**: 373, 1948).
† PBZ = pyribenzamine.

The fact that psychological factors concerning the patient influence therapeutic results is generally well recognized. Somewhat less well appreciated is the fact that prejudice on the part of the physician may also greatly affect the data. The patient is usually given the new treatment along with encouraging, enthusiastic comments by the physician. While this represents the art of medicine, it does not represent the science of medicine, unless a control group is given a sugar tablet along with the same enthusiasm. Further, when the patient is being questioned and examined to determine whether the new drug was effective, it is very easy for the physician to influence the results unconsciously by the type of questions asked or by looking for the things he wants to see. There is a tendency for the investigator to look for the good in a drug if he is trying to discover a new cure and establish a scientific reputation. Conversely he may look for the bad in a drug if one of his scientific colleagues has "out-theorized" him and developed a new treatment and perhaps thereby won the Nobel prize. While this is obviously an overstatement, there is a certain amount of truth in the thought expressed that will be appreciated by those competing in scientific circles. The blind placebo helps to overcome these variables.

TABLE 3.—*Khellin in Angina* *

	Percentage of Days in Which Cardiac Pain Was Reported as			
	Unchanged	Increased	Reduced	Absent
Khellin	41.3	14.8	21.2	22.7
Placebo	46.2	15.5	20.3	18.0

* Adapted from Greiner and others (Am. J. Med. **9**: 143, 1950).

TABLE 4.—*Sulfonamides in Sore Throat* *

	Fever	Edema	Pain	Complications
Sulfanilamide	1.15 days	3.19 days	1.81 days	4%
"Sulfatriad"	0.85 days	2.58 days	1.85 days	15%
Lactose	1.07 days	3.12 days	1.95 days	9%

* Adapted from Landsman and others (Brit. M. J. **1**: 326, 1951).

TABLE 5.—*Zinc Ethylene Bis-Dithiocarbamate in Tinea Capitis* *

Medication	Number	Number Cured	Percentage Cured
Carbowax® (placebo)	35	29	82.9
Zinc ethylene bis-dithiocarbamate	59	48	81.4

* Adapted from Kligman and Anderson (J. Invest. Dermat. **16**: 155, 1951).

Data to illustrate the "therapeutic potentialities and the toxicity of the placebo" are submitted in tables 1 to 5. It is obvious that if placebos had not been used to control these studies the conclusions drawn might have been entirely different and inaccurate. It is hoped that this bit of "propaganda" will contribute something, no matter how small, to the cause of controlled drug investigation in man.

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USE AND ABUSE OF BLOOD TRANSFUSIONS

To the Editor:—The article "Use and Abuse of Blood Transfusion," by Drs. B. Straus and J. M. Torres, in THE JOURNAL, Feb. 28, 1953, page 699, is timely and practical. The warning that blood must be conserved and that indications for transfusion should at all times be clear cut cannot be given too often, and I agree with the authors in their conclusion that ". . . a greater respect for the dangers of transfusion and attention to proper indications . . . will result in fewer accidents and diseases secondary to this procedure."

I wish to point out, however, that the limitation of the number of transfusions given in a period of time will not of itself reduce the frequency of reactions and transmission of disease. Accidents can be reduced to a logical minimum only

by careful observance of established principles of good use of the blood bank, from careful selection of donors and collection and preservation of blood to correct grouping and crossmatching and careful administration to the recipient.

We should like to suggest further that the practice of sending to the ward or operating room all the blood ordered for the patient is, in most instances, unnecessary and is responsible for both outdating and errors when the blood is returned to the bank.

Finally, we must take exception to the implication that our large blood centers, by using as donors "malnourished, homeless persons who must sell their blood to live," and "by their cursory examination given these donors . . ." are responsible for transmission of disease. The standards set by the large blood centers themselves and the steady raising of these standards by organizations such as the American Association of Blood Banks and especially by governmental agencies, such as the National Institutes of Health, the state departments of health, and finally, on the local level, the city departments of health, afford ample protection against such abuses. Without these large "blood centers," we could not supply nearly enough blood for transfusion and preparation of blood derivatives. They operate under licensure and inspection by the agencies named and must therefore select donors in accordance with regulations. That they are doing just that may be seen from the following figures, taken from the annual report of a representative community blood bank (Blood Transfusion Association, New York City) for one year.

Donors accepted	17,520
Donors rejected on interview	13,614
Donors rejected by physician	1,200
Positive serologic tests	184
Abnormal chemistry (serum bilirubin, cephalin flocculation, thymol turbidity)	66 (6 months)

It would appear from these figures, therefore, that "many apply but not all are taken."

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INTERPROFESSIONAL RELATIONS

To the Editor:—As a pharmaceutical detail man with almost seven years' experience in central Massachusetts, I have a suggestion to offer that might bring about a more harmonious practice of medicine. In my work, I have seen and still do see many instances of friction and "minor" irritation between physicians and druggists that have no justification for existence. A few examples include (*a*) "counter prescribing" by druggists, (*b*) dispensing by physicians, (*c*) duplicating products prescribed by physicians, (*d*) dispensing unwanted brands by druggists, and (*e*) quoting prescription prices by physicians. I find myself, like many other detail men, placed in the position of being a buffer and sometimes even a scapegoat between the professions of medicine and pharmacy, and, since my livelihood is directly dependent on both groups, my only interest is to see that they prosper in as pleasant a relationship as possible.

I believe that a rather simple solution exists, and, although it may not be complete in itself, it may lead to that end eventually. I suggest a panel discussion meeting between the organizations on a local level, with the detail men's organization taking an equal and active part. This type of meeting is easy to arrange and would need no more than two members of each organization on the panel and an objective moderator (perhaps even a detail man). Each member of the panel could be allowed a short time to expound his views on any given subject, and then questions from the audience could be directed at the panel. A meeting of this type, properly supported by and publicized to the respective organizations, would be sure to arouse interest by the very nature of its controversial features. The fact that physicians must attend too many meetings of one type or another would not materially affect their attendance at such a panel discussion, because the problems at hand vitally concern them. This sort of meeting would bring these problems into the light of open discussion and perhaps result in their solution. As long as the moderator could maintain decorum and eliminate emotion, such a meeting would be an invaluable experience to all concerned.

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MILITARY PREVENTIVE MEDICINE SOCIETY IN KOREA

To the Editor:—Among the more regular journals reaching us in Korea is The Journal, wherein, under Government Services, we see announcements of various societies meeting in Korea. I am taking the liberty of mentioning that the Military Preventive Medicine Society in Korea, on Jan. 14, held its first anniversary meeting. The society serves a dual purpose. In its monthly meetings, the morning session is devoted to unification of administrative matters among the army, corps, and division preventive medicine officers and the entomologists and sanitary engineers of the preventive medicine company and control detachments. Also in attendance are representatives of the hygiene section of the commonwealth division, ROK personnel, and UNCACK health officers. The afternoon session begins with a short business meeting, and the remainder of the time is given to a guest speaker. At the first anniversary meeting the guest speaker was Lieut. Col. Irvine H. Marshall (MC), a physician and diplomate of the American Board of Preventive Medicine, who was the founder of the society and who for the past 18 months has been chief of preventive medicine for the Eighth Army.

We all feel that the services of preventive medicine have been noteworthy in the Korean action. Colonel Marshall discussed the year 1952 in preventive medicine in Korea and illustrated his remarks with charts showing a good record in the control and elimination of communicable disease, insect-borne and rodent-borne diseases, and other phases of the work. We have many visitors from the states who have been interested in preventive medicine. We are always glad to have interested persons "drop in," and I would like to extend such an invitation to all who may be coming here.

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SENSITIVITY TO COMPOUND G-4 ("DICHLOROPHENE") IN DENTIFRICES

To the Editor:—In the March 21, 1953, issue of The Journal, page 998, there is a report by A. A. Fisher and Louis Tobin of four cases of allergic dermatitis and cheilitis due to G-4, dihydroxydichlordiphenylmethane. During World War II we performed "prophetic patch tests" with this compound, which was being considered for use as an antimildew in fabrics to be used by our armed forces. The percentages in the fabrics was 0.45% of weight of fabric. A total of 232 subjects were patch tested, and eight reactions were obtained. As a result its use was disapproved by the U. S. Army Industrial Hygiene Unit. The hexachlorophene compound G-11 was found to be safe for such use. Schwartz, Tulipan, and Peck (Occupational Diseases of the Skin, Philadelphia, Lea & Febiger, 1947, p. 298) list dihydroxydichlordiphenylmethane as a skin irritant in concentrations as low as 0.45%. These facts show that G-4 is not suitable for dentifrices, cosmetics, and wearing apparel and again prove the value of the "prophetic patch test."

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COUNCIL ON MEDICAL SERVICE

This is the ninth in a series of studies made by the Committee on Indigent Care of the Council on Medical Service concerning local plans for medical care of the indigent. A general introduction to the series appeared in the May 10, 1952, issue of THE JOURNAL, *pages 188-191. The eighth study (Polk County, Iowa) appeared in the Jan. 24, 1953, issue, pages 320-323.*

MEDICAL CARE OF THE INDIGENT IN RHODE ISLAND

The following is a study of the new plan for medical care of the indigent of Rhode Island, which began operation July 1, 1952. Owing to the brief period in which the plan has been in effect, data are not yet available concerning operating costs and the number of treatments provided. However, information concerning the administration, fee schedules, and the type of service available have been abstracted from the program manual published by the Rhode Island State Department of Social Welfare, with supplementary information supplied by the department.

Rhode Island, the smallest state in the union, had a population in 1950 of 792,000. Almost one-third of the state's residents, 249,000, live in Providence, the only Rhode Island city with more than 100,000 population. Approximately one-sixth of the state's population is engaged in manufacturing, and there are about 2,500 farms in the state.

ELIGIBLE POPULATION

As yet, there are no annual figures for the new medical care program. The number of persons receiving some form of public assistance in May, 1952, is shown in table 1.

TABLE 1.—*Number of Persons Receiving Public Assistance in May, 1952*

General Assistance		11,367	(5,287 families)
Public Assistance		17,841	
Old Age Assistance	9,361		
Aid to Blind	184		
Aid to Dependent Children	8,039		(3,330 families)
Aid to Permanently and Totally Disabled	257		

Medically indigent residents are included in the general assistance figures. The total number of persons eligible for care under the plan is, therefore, approximately 29,208, or 3.7% of the state's population.

ADMINISTRATION

Before the present plan was inaugurated, the great majority of medical care for assistance clients was provided through payment to the clients themselves, although some payments were made direct to the providers of this care from general assistance funds. The new plan places all care for public assistance clients under the supervision of the Division of Public Assistance of the state's Department of Social Welfare, while general assistance clients receive care through the Department of Public Welfare of the community in which they reside. The medical director of the Division of Public Assistance exercises over-all authority and supervision of medical care provided.

Assistance clients are eligible for medical care without further authorization, provided that there are no other resources they can utilize, such as relatives, insurance plans, or agencies organized to provide for victims of specific illnesses. The manual points out, "Since Public Assistance is supplementary to personal and community resources and should never supplant these resources, they are to be utilized to the fullest extent possible in order to preserve maximum personal and community responsibility." Social workers of the Division of Public Assistance determine if such resources are available or if public funds are needed to meet the client's medical expenses.

The medically indigent, though not clients of any specific assistance program, may obtain aid in the payment of medical costs by applying to the local welfare department within 30 days after the need first arises. This local office also acts as an information center for physicians and others providing medical care and supplies who wish to determine a patient's eligibility for public care. Forty-two of these offices serve the 15 districts into which the state is divided; the district offices are under the direct supervision of five "area offices," which are, in turn, responsible to the state office in Providence.

Advisory committees of the Rhode Island Medical Society, the Hospital Association of Rhode Island, the Rhode Island State Dental Society, the Rhode Island Optometric Association, and the Rhode Island Chiropody Society and an Advisory Committee on Pharmacy cooperated in formulating the program and in establishing fee schedules for the various services. A continuing liaison is maintained between the Department of Social Welfare and the various professional groups, and the advisory committees may be consulted concerning problems arising in their respective fields. Appeals by physicians and other personnel providing medical care may be made directly to the medical director or to the appropriate advisory committee or both. A fair hearing process has also been established by the state for assistance clients who wish to appeal an agency action.

SERVICES AVAILABLE

Medical care, as defined by the manual, includes "those basic medical services and supplies, in essential quantity, at minimum adequate cost, which are required for the diagnosis, treatment and control of sickness or injury, to the end that physical, mental and economic self-help may be achieved to the maximum possible for each needy person requiring such medical care."

Fourteen medical services are listed as falling within the scope of the program: services of physicians, consultants, dentists, chiropodists; x-ray and laboratory services; eye care and glasses; appliances; drugs; ambulance service; hospital, clinic and convalescent care; and home nursing. The services are available to all assistance clients and to the medically indigent, whenever they are not otherwise obtainable.

The client may be treated by the physician of his choice in the home or office; prior authorization is required only if more than eight visits per month are needed, in a case of acute illness, or more than two visits per month, for chronic illness. In emergencies, treatment above these limits is permitted without prior authorization. The program covers prenatal and postnatal care in home and office, but hospital delivery is expected, except in cases of emergency.

Usually, provision is made for the services of only one physician at a time. With prior authorization, however, a single office or home visit by a consultant is allowed; in emergencies, the prior authorization is not required.

On the recommendation of the attending physician, a client may be hospitalized in any approved voluntary hospital in the state. Ward accommodations are utilized, and all ordinary hospital services are provided, including maternity care. Hospitalization outside Rhode Island, within the cost standards of the plan, is provided when the service required is not available in the state or if the patient is outside the state when the need arises.

No change has yet been made in methods of providing clinic care; pending a thorough study of the situation, local welfare departments maintain the same arrangements with local clinics as were in force prior to the beginning of the new program. Care is provided at licensed convalescent and nursing homes if needed services are not available at the state infirmary or other sources. On recommendation of the attending physician, clients may also receive home care from registered nurses or licensed practical nurses.

Within the limits of the manual's definition of medical care, dental care in the dentist's office is also provided. All types of dental work are covered, including oral surgery, extractions and bridge work; at present, orthodontia is excluded. Prior authorization is required only for work costing more than $15; for work costing between $15 and $50, the authorization is based on x-ray examination of the specific area to be treated,

while for work costing more than $50, a full mouth x-ray examination is required before authorization.

Treatment by licensed chiropodists is provided without prior authorization up to a maximum of five home or office visits per month for acute conditions and two per month for chronic conditions. For treatment beyond these limits, prior authorization is required.

Diagnostic x-ray services, as well as x-ray and radium therapy, must be provided by an approved radiologist. Diagnostic services may be provided without prior authorization, but authorization is required for either type of therapy, which will be provided only when other resources cannot be utilized, whether because of distance limitations or other reasons. Payment for diagnostic x-ray services will be allowed to physicians other than approved radiologists only in emergency cases.

Laboratory services are provided by clinical laboratories approved by the State Department of Health and the Public Assistance Office of Medical Service. The program encourages the use of existing public health laboratory facilities and the "diagnostic battery of laboratory tests" which the private laboratories usually provide. The only authorization needed for such services is a written statement by the attending physician that such tests are necessary.

Physiotherapy may be provided in home, office or hospital, but is considered part of the professional services rendered by physician or hospital rather than a separate service.

Complete eye care is provided, including examination, refraction and diagnosis; new eye-glasses may be obtained or old ones replaced or repaired. Payment is provided for professional care by any licensed ophthalmologist or optometrist and for filling of their prescriptions by opticians.

Surgical and prosthetic appliances are provided on the recommendation of the attending physician; prior authorization is required in each case. Ambulance service is provided when essential for transporting a patient to or from a hospital.

Drugs may be obtained from licensed pharmacists upon the written prescription of the attending physician, with the exception of expensive or experimental drugs of doubtful efficacy or drugs in the state of preliminary trial. Drugs provided by the physician or the hospital are considered part of the professional services rendered.

PROVIDERS OF SERVICE

No figures are as yet available as to actual participation in the program, due to the short time it has been in operation. However, no participation agreements are required, so that any licensed physician may provide the service. In 1950, approximately 950 physicians were in practice in Rhode Island, including over 300 specialists. There are approximately 95 private duty nurses and 152 practical nurses in the state.

The program provides for care in public hospitals only when the client is hospitalized outside the state; therefore, the 16 nonprofit private hospitals, with a total of 2,420 beds and 432 bassinets, provide all hospital care for clients of the program.

PAYMENT FOR SERVICES

Through consultation with the advisory committees of the professional groups concerned, fee schedules have been established for most of the services provided. In general, only one agency or supplier is paid for each service rendered. Physicians are paid for home and office visits but not for hospital visits; only the hospital receives payment for hospital or outpatient department care. Drugs and physiotherapy provided by physicians and hospitals are considered part of the professional services rendered and are included in the flat rate paid for such care.

Physicians are reimbursed at a rate of $3.00 for office visits, $4.00 for home visits during the day, and $5.00 for home visits at night. For additional patients seen during a single visit, $2.00 is allowed, with a maximum payment of $7.50 per visit. The maximum payment for minor surgery in home or office is $10.00. Consultants receive $5.00 for office visits and $10.00 for home visits.

The ordinary maximum per diem allowance for hospital care is $14.00 and for infants after delivery $3.00 per diem is allowed. Prior authorization is required for hospitalization costs that exceed this rate.

Payments for clinic care are determined in accordance with the previous agreements between the institution and the local welfare department; if the clinic has been providing this care gratis, it will continue to do so, pending the completion and study of a survey being conducted by the Hospital Association of Rhode Island. Payments for convalescent and nursing home care are determined by public assistance cost standards for the type of care provided and, in the case of home nursing, by the hours of service required.

A detailed fee schedule has been established for dental work, with fees ranging from $2.00 to $75.00, depending upon the type of work done. Chiropodists are paid $2.00 for office visits, $3.00 for home visits during the day, and $5.00 for home visits at night. Allowances for clinical laboratory services range from 50 cents to a high of $6.00, for a basal metabolism test.

Drugs are paid for at the unit cost price plus 50%, except drugs which have fair-traded minimum retail prices, in which case these prices apply. If compounding of at least one-half hour's duration is involved, a higher rate of payment for the prescription may be authorized. Cost standards for appliances will be established after the program has been in operation six months, so that payments may be based on experience in the type and number of appliances needed.

The method of payment varies somewhat with the type of service. For all services except clinic, convalescent and nursing home care and home nursing, bills are sent to the agency

TABLE 2.—*Vendor Payments from General Assistance Funds for Indigent Medical Care, Fiscal Year 1952*

	Hospital Care		Medical Care	
General Assistance Clients	$197,432		$48,151	
Public Assistance Clients	268,932		17,145	
Old Age Assistance		$179,406		$7,970
Aid to Dependent Children		84,097		8,748
Aid to the Blind		3,092		206
Aid to the Permanently and Totally Disabled		2,337		221
Total	$466,364		$65,296	

concerned. Bills for public assistance clients are sent to the State Public Assistance Office of Medical Service in Providence and for general assistance and medically indigent clients to the local department of public welfare. Most bills are due by the 10th day of the month following that in which service is provided.

For clinic care, the bill is sent to the local welfare department; for convalescent and nursing home care and for home nursing, the bill is given to the client, with the physician's recommendation as to the future care needed. The client gives this information to the social worker handling his case, who arranges the necessary increase in the total amount of assistance paid the client. The client then pays the home or nurse from this increased allotment.

COSTS AND FINANCIAL SUPPORT

Public assistance medical care is supported by state and federal funds, through a "pooled fund" arrangement, as allowed by the 1950 amendments to the Social Security Act. The state and federal funds provided for public assistance are pooled, and a monthly assessment for medical care is made from this fund for each public assistance client. This medical care fund is then utilized to pay medical bills for all clients of the program. General assistance medical care costs are met by local funds, with the state reimbursing local government for 70% of such costs.

As yet, insufficient data has been acquired to enable a tabulation of total costs or expenditures per client for the new program; however, cost figures for the fiscal year 1952, immediately prior to the inauguration of the new program, may serve as an indication of possible expenditures under the new plan. During this period, medical care was reimbursed by two methods: direct payment to the vendor from general assistance funds and inclusion of medical care payments in the client's regular assistance check, with the client paying the vendor. The figures given represent only the payments direct

to vendors from general assistance funds and, therefore, show only one-third or less of the total cost of medical care for the indigent, according to the state welfare department. In addition to the costs given in the table, $1,764 was paid for ambulance service for assistance clients.

From the figures given, it can be seen that the total vendor payments for indigent medical care during the year were $533,424. Using as the number of eligible clients 29,208, the average payment would be $18.26 per eligible client. If, as is estimated, this amounts to only a third of the total cost, then total expenditures for indigent medical care during the year were approximately $1,600,000, or about $54.75 per eligible client. It cannot, as yet, be determined how closely costs under the new program will approximate these figures.

MEDICAL SOCIETY RELATIONSHIP

The program was drawn up with the assistance of the committee on social welfare of the Rhode Island State Medical Society, which also aided in formulating the fee schedule for physicians' services. It is apparent, therefore, that the state society was actively interested in the establishment of the plan and will continue to aid in its development. The social welfare committee continues to work with the state welfare department in an advisory capacity and has been called upon frequently by the medical director for advice and assistance in coping with problems not specifically covered by the established standards and regulations. Information is not yet available on the amount of participation in the program by individual members of the society.

SUMMARY

Since the Rhode Island program for medical care of the indigent is barely eight months old, its efficacy cannot be fully determined. However, the plan seems a firm basis for efficient handling of this problem.

Public assistance care is administered by the state Public Assistance Office of Medical Service, except clinic care which, like general assistance medical care, is administered by local welfare departments. Thus medical care is, in general, provided through the same department, state or local, as is other assistance, and administrative complexity is kept to a minimum. This not only makes actual management of the program easier but also makes the cost of each program more readily determinable than in the former plan, when medical care was provided either through general assistance funds or by increases in the regular assistance checks.

In general, clients of any assistance program are eligible for all forms of care without prior authorization, except when the treatment will be overly expensive or prolonged. The program manual states that "the decision as to the specific medical needs of each patient is a professional one. Public Assistance is concerned (only) with the financial need. . . ." This is borne out by the fact that, for all services except the few requiring prior authorization, the recommendation of the attending physician is the only requirement.

Patients have free choice of physician and of all other vendors of service or professional personnel within the scope of the program: the only limitation is that assistance funds will be used to pay for medical care only when the client cannot obtain this care from any other source. In this way, the program avoids duplication of the services provided by public health agencies and various voluntary organizations.

Fees are somewhat restricted, in that physicians are reimbursed for home and office care at a set rate, regardless of service, and are not paid for treatment in hospitals or hospital outpatient departments. Hospitals are paid a flat per diem rate for all services, including drugs and physiotherapy. Prescriptions are filled by private pharmacists on a cost-plus basis, with fair-traded drugs provided at the minimum retail price.

Cost standards have been established for all services except clinic care, where prevailing standards in the individual communities remain in effect pending a state-wide survey by the welfare department and the hospitals of the state. Cost standards for surgical and prosthetic appliances will be developed after six months of experience with the plan. Owing to the short time the program has been in operation, figures are not available for total expenditures or cost per eligible client.

The Rhode Island State Medical Society, as well as the other professional groups concerned, has had an active part in the formulation of the program and continues in an advisory capacity to the medical director; the welfare department plans to concern itself solely with the financial and administrative aspects of the plan and to leave medical care in the hands of the private physician. Indeed, the medical director of the program has stated that Rhode Island is "not attempting to set up a 'police body' to supervise . . . methods of practice" but to provide this care for the indigent on a more effective basis.

In general, the program seems designed to provide adequate care for the needy of the state and at least some reimbursement for the professional providers of this care. Only experience, however, will show how effectively this goal is attained.

COUNCIL ON NATIONAL EMERGENCY MEDICAL SERVICE

RESULTS OF SURVEY OF DISCHARGED PHYSICIANS

Some time ago the Council on National Emergency Medical Service initiated a survey of physicians being separated from active military service. In advance of a complete tabulation of the questionnaires received to date, a preliminary review has been made of the questionnaires received from physicians separated from active military service since June 1, 1952. A total of 467 questionnaires were analyzed to obtain information with respect to (a) *the percentage of time spent by physicians in the treatment of military personnel and their dependents;* (b) *staffing conditions; and* (c) *the reasons given by physicians who have indicated that they would be willing to serve beyond the required period of 24 months. A detailed analysis of this information is indicated below.*

C. JOSEPH STETLER, *Secretary.*

Percentage of Time Spent in Treatment of Military Personnel and Their Dependents

	Military Personnel		Dependents of Service Personnel	
	Overseas	Domestic	Overseas	Domestic
Army	54	53	28	26
Navy	54	46	19	25
Air Force	44	39	19	44

Staffing Conditions on Last Assignment

	Over-staffed		Under-staffed		Adequate	
	Replies		Replies		Replies	
	No.	%	No.	%	No.	%
Army	16	15	30	28	63	58
Navy	93	34	40	15	138	51
Air Force	27	44	9	15	26	42

Willing to Stay in Service

	Yes	No
Army	48	59
Navy	137	142
Air Force	29	35

Conditions Under Which Physicians Would be Willing to Stay in Service

	Army	Navy	Air Force
Total war	5	6	1
Higher rank	1	1	..
Less dependent care	2	7	6
Better utilization	1	7	1
Opportunity to practice specialty or better assignment	4	2	..
Better rotation policy	3	1	..
Miscellaneous reasons	6	17	5
No reasons given	26	96	16
Total	48	137	29

COMMITTEE ON MEDICOLEGAL PROBLEMS

The Committee on Medicolegal Problems of the American Medical Association has approved the publication of the following report prepared by Alexander S. Wiener, M.D., with the assistance of David N. W. Grant, M.D., Lester J. Unger, M.D., and William G. Workman, M.D.

J. W. HOLLOWAY JR., *Secretary.*

MEDICOLEGAL ASPECTS OF BLOOD TRANSFUSION

During the past few decades vast strides have been made in the practice of blood and plasma transfusion. Blood transfusion has become a safer and less unpleasant procedure for the patient as a result of two advances: firstly, the discovery of the Rh factor, which led to new tests for the detection of intragroup incompatibilities, and secondly, the discovery of the cause of pyrogenic reactions and the development of methods of preventing them. The introduction of blood banking, which has been greatly expanded in recent years, thanks to the invention of inexpensive and reliable expendable transfusion equipment for the collection, storage and administration of blood, has greatly increased the ready availability of blood and plasma. Accordingly, today blood and plasma transfusions are almost as commonplace as ordinary sodium chloride and glucose infusions. This has made possible major surgical procedures previously too dangerous to undertake, and has also reduced markedly the frequency of deaths from hemorrhage.

Because of the ease with which transfusions can be carried out, there has been a tendency to overlook the fact that blood and plasma transfusions are attended with certain dangers which are not shared by simpler intravenous procedures. Recent reports [1] estimate the mortality from blood transfusion at the present time, even at the best-run institutions, to be approximately 1 death in 1,000 to 3,000 transfusions. Considering that as many as 3,500,000 transfusions may be given annually in this country,[2] this makes blood transfusion as important a cause of death as appendicitis or anesthesia. It is the ethical and legal responsibility of all physicians and hospitals to take every precaution possible to safeguard the patient against these dangers. The purpose of this report is to review the untoward sequelae which may follow blood and plasma transfusions, and the steps which can be taken to avoid these dangers. While the recommendations presented here are intended as a guide to physicians performing transfusions, allowance should be made for changes that may become necessary as new information becomes available.

HEMOLYTIC TRANSFUSION REACTIONS

One might imagine that at the present stage of knowledge hemolytic reactions caused by incorrect grouping of blood should no longer occur. However, there are circumstances under which errors may occur, namely, in times of unusual emergencies when incompletely trained individuals are called upon to perform such tests. This could occur not only in the event of national emergency, but also in peacetime. For example, when emergencies arise in the middle of the night or on holidays and the trained technician is not at hand, persons who have not been fully trained may be called upon to perform the grouping and cross-matching tests, and a certain number of errors are then inevitable. All hospitals should carry liability insurance. In addition, it is recommended that medical schools devote more attention to blood grouping in their curricula, so that interns and other young physicians who may be called upon to perform these tests in emergencies will be better equipped to do so.

A certain number of errors resulting from human fallibility are inevitable, but these should be kept at a minimum. Mistakes have resulted because blood grouping serums have inadvertently been interchanged; or when two patients have required transfusions at the same time, occasionally the bottles of blood intended for them have been interchanged. One of two patients with very similar or identical names may require a transfusion; in such cases also blood has been administered to the wrong person. In a few cases, errors have resulted because the wrong pilot tube was affixed to the bottle of blood. Most transfusions of blood of a wrong group can be traced to failure to read labels. A procedure should be set up in every hospital requiring that no technician may proceed with the blood grouping tests until he has read the labels on each bottle of grouping serums and every specimen of blood, and until he has established the identity of the patient receiving the blood. Colored grouping serums and labels have the disadvantage that the technician has a tendency to rely on his memory of the colors instead of reading the labels on the bottle of blood to be administered.

If a patient dies as a result of a transfusion of blood of an incorrect group, or suffers a prolonged illness due to injury to his kidneys, the patient's family or the patient himself, if he survives, may be entitled to damages unless there were extenuating circumstances calling for rapid action. Here the doctrine *res ipsa loquitur* may be applicable, because transfusion of an incompatible group at the present stage of knowledge may be considered prima facie evidence of negligence.

A-B-O Blood Groups.[3]—One of the commonest causes of hemolytic reactions is the transfusion of blood of an incompatible blood group. This may seem surprising considering that high-titered and specific blood grouping serums are now readily available, so that with care errors in blood grouping should hardly ever occur.* When carrying out blood grouping tests, it is important not only to test the patient's red blood cells with potent grouping serums anti-A and anti-B, but also to check the patient's plasma for its isoagglutinin content against known cells of group A and B.† While this check is not available when grouping blood from newborn babies, it is a valuable control on the results for older children and adults, and therefore should not be omitted. As an additional safeguard the bloods of donors and patients must be cross-matched by an acceptable technique.

No doubt, transfusion of blood of an incorrect blood group occurs far more often than the recorded instances. Natural anti-A and anti-B isoantibodies in human serums are generally of low titer and avidity, so that an initial transfusion of group A blood to a group O individual, for example, may be uneventful or give rise to a reaction from which the patient readily recovers. As a result of such a transfusion of incompatible blood the isoantibody titer will rise, so that if the error is repeated a fatal reaction could result. The titer and the avidity of the isoantibodies may be high, moreover, in individuals who have received previous transfusions of pooled human plasma or after heterospecific pregnancies, e. g., mother group O and baby group A, or after injections of horse serum or vaccines of bacteria grown on media containing peptone prepared with hog pepsin. In such instances, the very first transfusion of blood of an incompatible group may give rise to a severe hemolytic reaction, followed by anuria and death.

The severity of the reaction in strongly sensitized individuals depends on the amount of blood transfused, fatalities in adults being infrequent with quantities of blood less than 300 cc.

Because of lack of space, some of the bibliographic references have been omitted from THE JOURNAL and will appear in the committee's reprints.

Acknowledgment is made of the comments and suggestions received from the following consultants: S. T. Gibson, M.D., R. S. Muckenfuss, M.D., R. Murray, M.D., and I. B. Wexler, M.D.

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1*c*. Straus, B., and Torres, J. M.: Use and Abuse of Blood Transfusion, J. A. M. A. **151**: 699-701 (Feb. 28) 1953.

2. Dickinson, F. G., and Welker, E. L.: Survey of Blood Banks in the United States and Possessions: A Report to the Committee on Blood Banks, Bulletin 75, Chicago, American Medical Association, 1950.

3. Davidsohn, I.; Levine, P., and Wiener, A. S.: Medicolegal Application of Blood Grouping Tests, J. A. M. A. **149**: 699-706 (June 14) 1952.

* Minimum requirements for blood grouping serum and anti-Rh typing serum are issued by the National Institutes of Health. Copies may be obtained upon application to the Laboratory of Biologics Control, National Institutes of Health, Bethesda 14, Md.

† The group A cells used should preferably be of subgroup A_1, in order to detect weak anti-A isoagglutinins.

Therefore, if the first portion of each unit of blood is given slowly and the patient watched closely during that time for untoward symptoms it may be possible to interrupt the transfusion in time, should a reaction develop. This safeguard is not available, of course, for patients under anesthesia. The increasing use of blood in the operating room for patients under anesthesia makes it necessary to emphasize one's complete dependence in such cases on the laboratory.

It has been claimed that the immediate symptoms of a hemolytic transfusion reaction may be suppressed while the patient is under cortisone or corticotropin (ACTH) therapy. However, hemolysis and hemoglobin nephrosis resulting in death is not prevented, so that such therapy does not eliminate the necessity for accurate grouping and cross-matching tests.

Subgroups of A.—It is important for the technician to be familiar with the subgroups of A in order to avoid errors in blood grouping. There are two principal forms of the agglutinogen A, namely, A_1 and A_2, the latter being characterized by its weaker reactions with anti-A serums. The reactions are especially weak in the presence of agglutinogen B, so that blood of subgroup A_2B (frequency of about 1.5%) has often been incorrectly classified as group B. (Bloods of subgroup A_3 and A_4, which are very rare, react even more weakly with anti-A serums.) The low avidity of most anti-A serums for A_2B blood which is responsible for errors in blood grouping also protects the patient receiving such incompatible blood from any dangerous reaction. That may be the reason why no serious transfusion reactions are known to have been traced to such a mistake in blood grouping. Nevertheless, in a well-regulated laboratory such errors should not occur. Although individuals of subgroup A_2 may occasionally have weak irregular isoagglutinins for subgroup A_1 and vice versa, no serious transfusion reaction has ever been traced to this source. For practical purposes, therefore, the subgroups of A are disregarded for blood transfusions, and donors are selected on the basis of the four blood groups.

Rh Factor.[3]—It has been found that it is not sufficient for recipient and donor to belong to the same A-B-O blood group, and today donors are routinely selected also on the basis of the Rh factor. Actually, the Rh-Hr types are quite complicated and reagents have been developed for as many as four different Rh factors and at least two Hr factors. For blood transfusion practice it is sufficient to limit the tests to only one of the Rh-Hr factors, namely, Rh_0,[4] the factor which corresponds to the one originally discovered with the aid of the anti-rhesus immune animal serums.

The Rh types differ from the A-B-O groups in that isoantibodies against the Rh-Hr factors do not occur in human serums except when induced by isosensitization. Therefore, generally, the initial transfusion of Rh-positive blood into an Rh-negative recipient is symptomless. In individuals who have been previously sensitized as a result of an injection of Rh-positive blood or a pregnancy with an Rh-positive fetus, even the first transfusion of Rh-positive blood can cause a severe reaction. The Rh_0 factor is highly antigenic, so that about half of the Rh-negative individuals transfused with Rh-positive blood may become sensitized, and if the injections of Rh-positive blood are repeated over a long enough period of time eventually almost all Rh-negative persons may become sensitized. When isosensitization occurs in an Rh-negative woman this may prevent her from having a normal child, should her husband be Rh positive, especially if he is homozygous. That is another reason why Rh testing has become routine before blood transfusions, namely, not only to prevent hemolytic reactions but also to avoid the development of isosensitization which may cause erythroblastosis fetalis in subsequently born children.

The other Rh-Hr factors are much less antigenic than Rh_0, so that ordinarily they are disregarded when selecting donors for transfusion. By carrying out cross-matching tests by one of the modern techniques designed to detect "univalent" antibodies, e. g., the conglutination method, the anti-globulin method, or the test with enzyme-treated cells, incompatibilities with respect to the other factors of the Rh-Hr systems can be detected should isosensitization be present. Therefore, at least one of these tests should be included in the cross-match routine. While it is not essential, it is considered good practice to test all prospective Rh_0-negative donors further with anti-rh′ and anti-rh″ serums, and to consider only type rh blood (triple Rh negative) Rh negative for transfusion purposes, in order to avoid the possibility of sensitization against the factors rh′ and rh″. On the other hand, recipients belonging to type rh′, rh″, rh′rh″, as well as type rh should be considered Rh negative, because blood of these types lacks the most antigenic Rh factor, Rh_0.

Potent and specific anti-Rh_0 testing serums are commercially available, so that errors in Rh testing should rarely occur at the present time. Certain unusual blood specimens may offer difficulties in Rh testing, however, so that an accurate diagnosis can then be made only by a specialist. For example, variants of the Rh factors exist, of which the most important are the Rh_0 variants ($\overline{Rh}_0$).‡ Persons with blood possessing an Rh_0 variant may be incorrectly classified as Rh negative, unless special testing serums are available and special techniques such as the anti-globulin (Coombs') test are resorted to. Transfusion of blood containing an Rh_0 variant into an Rh-negative recipient can give rise to isosensitization, just like typical Rh-positive blood. On the other hand, under certain conditions, Rh-negative blood may seem to react as Rh positive. For example, if bloods from pregnant women are tested by the slide technique, rouleaux formation which occurs in pregnancy may be mistaken for clumping. In acquired hemolytic anemia, the red blood cells may be coated with autoantibodies, which may be responsible for clumping in tests carried out by the conglutination method. Of course, these difficulties apply primarily to patients and not to healthy prospective donors. When the results of a slide Rh test are unclear, the test should be repeated by the tube agglutination method.

In most cases where Rh-positive blood is transfused to Rh-negative individuals, this can be traced to some error rather than a peculiarity in the blood to be tested. At the present stage of knowledge, if a hemolytic reaction occurs due to a transfusion of Rh-positive blood to an Rh-negative patient, it is generally prima facie evidence of negligence. The physician and hospital should make certain that all Rh-negative patients receive only Rh-negative blood, not only to prevent reactions, but also to avoid the development of isosensitization in women capable of child bearing. (This rule is not applicable in cases of dire emergencies, as is discussed later on.) Court actions have been initiated by women who had stillbirths which they traced to isosensitization produced by an earlier transfusion of Rh-positive blood.

Thus, the selection of donors for transfusion is no longer the simple procedure it was a few years ago. With the realization of the importance of the Rh-Hr factors, and the introduction of new complicated blood typing and cross-matching procedures, it has become necessary to relegate this work to specially trained individuals. Every blood bank and hospital where blood transfusions are carried out should have such specially trained technicians to handle this work under qualified medical supervision. Only in that way can maximum safety for the patient requiring blood transfusion therapy be obtained.

"Universal" Donors.—While transfusion of group A blood into a group O recipient may cause a serious reaction, the transfusion of group O blood into a group A recipient is generally harmless. The reason for this is that in the former case a relatively small volume of incompatible donor's cells combine with the isoantibodies present in a much larger volume of the recipient's plasma, while in the latter instance a limited amount of incompatible donor's plasma is diluted in the recipient's circulation and absorbed by the great mass of the patient's red blood cells. In general, therefore, blood containing incompatible agglutinins is much less dangerous than blood containing incompatible agglutinogens, and that is the basis for the use of group O individuals as so-called "universal" donors. The advantage of the use of universal donors is that by selecting such group O donors ahead of time by careful grouping tests done at leisure, time is saved in emergencies. This eliminates the danger of errors in blood grouping, which are particularly prone to occur when tests are carried out

‡ Rh_0 variants have also been referred to by the symbol D^u.

hurriedly or by poorly trained technicians. For this reason in England at one time only volunteer donors of group O were used for blood transfusion. This policy was abandoned primarily because a shortage of blood was created by the failure to use donors belonging to the other blood groups, A, B, and AB.

It is now known, moreover, that transfusion of group O blood into individuals of other groups may occasionally be dangerous. Hemolysis may follow such transfusions when the donor has isoagglutinins of high titer in his serum. In a number of cases this has been traced to the use of donors who had recently received injections of tetanus antitoxin prepared in horses (cf. page 1435 under A-B-O Blood Groups).

While the injection of high-titered group O blood into individuals not belonging to group O may produce an acute hemolytic reaction, the symptoms are usually somewhat different from those which occur when incompatible red blood cells are injected. When potent incompatible antibodies are introduced they coat the recipient's red blood cells and an hemolytic process develops, which may continue over a period of days, producing a clinical picture resembling that of acquired hemolytic anemia. Therefore, it is preferable to transfuse only blood of the same group as the recipient whenever such group specific blood can be made available. The use of group O blood as "universal" donor blood should be restricted to emergencies where there is not enough time to determine the blood group of the recipient reliably. When more than a single unit of group O blood has to be administered to a patient not belonging to group O, one must bear in mind the possibility of a cumulative effect from the incompatible isoantibodies. Except under extraordinary emergencies, while the first unit is being administered there should be ample time to group the patient in order to select blood of the patient's own group, should additional transfusions be required.

To provide for emergencies the titer of the isoagglutinins in group O blood should be determined, and those units of group O blood with low titers may be marked for use as "safe" universal donor blood. The simplest method is to screen out those group O bloods with isoagglutinin titers which in the experience of the laboratory would be included among the highest 10 to 30%, and to use only the group O bloods with lower titers for this purpose. The value of the use of A and B blood group substances in this connection has not been clearly established. When an emergency makes the use of "universal" donor blood essential, a statement to this effect should be written on the hospital chart as a safeguard should a reaction result and a lawsuit be instituted.

In the case of emergency, of course, it is not feasible to carry out the delicate tests necessary to determine the Rh factor reliably. Routine Rh tests are usually performed during pregnancy on all obstetric cases, and the results of these tests can serve as a guide when selecting blood for such patients should an emergency arise during delivery. Where such information is not available and a dire emergency exists, preferably low-titered group O, Rh-negative blood should be used for transfusions, especially to women during the child-bearing period. If Rh-negative blood is not at hand, and the transfusion is deemed a life-saving procedure, Rh-positive blood may be used provided cross-matching tests show no incompatibility. Obviously, one must balance the danger of hemorrhage against the danger of isosensitization, and a suitable entry should be made on the patient's chart to justify the course of action taken.[5]

The transfusion of Rh-negative blood of the proper blood group into an Rh-positive recipient is almost always safe. The likelihood that such transfusions may give rise to sensitization to one of the Hr factors is so remote that for practical purposes this is generally disregarded. However, such instances, though rare, do occur, so that careful cross-matching tests must be done to detect incompatibilities aside from those due to the Rh_0 factor. Another source of danger is the possibility of introducing Rh-negative blood containing potent Rh antibodies into an Rh-positive recipient, thus causing an hemolytic process. Or the transfusion of such blood into an Rh-negative pregnant woman could passively sensitize her and in that way conceivably cause erythroblastosis in her baby. These dangers can readily be avoided by testing all Rh-negative donors for Rh antibodies, and eliminating those who are sensitized, though this has not yet become a regular routine at most blood banks.

Other Blood Groups.—The serums of certain rare individuals contain naturally occurring irregular isoantibodies for blood group factors other than A and B, e. g., anti-M, anti-P, and anti-Lewis. Such natural antibodies are generally of low titer and most active at low temperature, and therefore do not cause transfusion reactions.

On the other hand, as a result of isosensitization, immune antibodies to blood factors besides Rh-Hr may be formed, notably anti-M, anti-Kell and anti-Duffy. These immune isoantibodies can give rise to serious hemolytic reactions, but such instances are quite rare. By careful cross-matching tests, using appropriate special techniques, antibodies capable of causing a reaction can be detected, but the in vitro reactions are frequently very difficult to elicit. For example, the so-called Duffy factor can be demonstrated only by means of the antiglobulin technique. When a patient has had an unexplained hemolytic reaction not traceable to the A-B-O or Rh-Hr factors, his blood should be studied by a specialist in the field before additional transfusions are given. For this purpose there are certain blood grouping laboratories to which the blood can be sent; and, in fact, any of the workers in the field would welcome such specimens because they are valuable research material.

The committee does not believe that reactions caused by sensitization to one of the other blood factors can properly be a cause of action for a lawsuit, provided that the physician and hospital have exercised ordinary care to protect the welfare of the patient.

Damaged Blood.—If the blood used for transfusion has been damaged during storage, it may break down rapidly in the patient's circulation and give rise to a hemoglobin nephrosis. Blood should always be inspected carefully by a responsible person before being issued, and if hemolysis is detected should not be released.§ One should also bear in mind that red blood cells are sensitive to freezing and over-heating, so that contact with dry ice must be avoided, and no attempt should be made to warm blood prior to or during its administration. Blood that has been stored too long or improperly can also give rise to transfusion hemolysis. The expiration date of blood depends on the medium in which it is stored. The National Institutes of Health permit an expiration date of 21 days for blood stored in acid citrate dextrose solution.

Needless to say, blood should be kept cold from the moment it is collected until it is used. It should be stored in a refrigerator, set at 4 to 10 C (preferably 4 to 6 C). According to the requirements of the National Institutes of Health, the temperature must be recorded at least once a day. This is discussed again in connection with the problem of infected blood. If the blood is properly refrigerated during shipment, it can be safely shipped by plane to other parts of this country, or even across the ocean. Containers have been devised in which the blood can be packed and kept at the optimal low temperature during shipping.

TRANSMISSION OF DISEASE

A serious problem is the possibility of the transmission of disease from donor to recipient. (The reverse possibility, namely, the transmission of disease from recipient to donor prevails only when direct blood transfusions are given.) One of the most serious dangers at the present time is that of transmitting homologous serum hepatitis to the patient. This may occur once among 200 patients receiving transfusions,[1a] and may be responsible for the patient's death once among 6,000 transfusions.[1a] This danger is even greater following plasma transfusions.

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5. For a detailed description of an acceptable procedure for use in emergencies, see Civil Defense Technical Bulletin, TB-11-5, and TB-11-6, Federal Civil Defense Administration, November, 1952.

§ Adequate examination is not possible, once the blood has been agitated.

Homologous Serum Hepatitis.—Attention was called to this entity during World War II as a result of the extensive use of pooled dried plasma when treating battle casualties. (Previously the disease had been observed as a complication following the injection of yellow fever vaccine, stabilized with human serum, and following the use of therapeutic immune human serums.) After an incubation period which may vary from one to six months, jaundice appeared in certain of the patients receiving plasma transfusions. Investigation revealed that in other patients receiving transfusions of the same lots of plasma jaundice also developed, confirming the suspicion that the plasma was the source of the hepatitis.

Plasma for transfusion is prepared in large pools in order to make safe its use in emergencies for individuals of any blood group. By pooling plasma of all blood groups, exceptionally potent isoagglutinins present in a particular sample of plasma are diluted, and at the same time plasma of opposite groups mutually inhibit one another's isoagglutinins by virtue of the soluble blood group substances which plasma contains. On the other hand, pooling increases the hazard of homologous serum hepatitis, because the presence of the virus in a single sample of plasma will serve to contaminate the entire pool. Thus, a pool of 50 units of plasma would be about 50 times as likely to transmit the disease. Indeed it has been found that homologous serum hepatitis occurs in as many as 12% or more of patients receiving pooled dried plasma, as compared with an incidence of 1 in about 200 after transfusions of whole blood.

For the purpose of this discussion, the most important difference between homologous serum hepatitis and infectious hepatitis (catarrhal jaundice) is the mode of transmission. Unfortunately, there is no simple test by which a carrier of the virus can be recognized, and the presence of the virus in a plasma pool can be detected only by testing it on human volunteers. The use of surplus plasma in civilian practice after the war resulted in additional instances of homologous serum hepatitis. Since the plasma in these instances had to be used in emergencies to save lives when blood was not available, at least one court has held that homologous serum hepatitis after plasma transfusions is a calculated risk, and no damages were awarded.[6]

Experiments have been carried out which suggest that ultraviolet radiation destroys the virus of hepatitis. Following this work, the National Institutes of Health have required that pooled plasma must be irradiated before distribution, and this ruling is still in effect. More recent observations indicate that such irradiation may not always be effective. Irradiation is not applicable to whole blood. One should also bear in mind the hazard of hepatitis to donors and patients from contaminated lancets and needles, and to workers handling human blood and plasma.

Summarizing the available data, one must conclude that the problem of homologous serum hepatitis has not yet been solved. The danger is much greater when pooled plasma is used than when plasma or whole blood derived from a single individual is administered. There is no practicable test to detect carriers of the virus, and the ability to transmit the virus may be retained for an indefinite period of time. Individuals with a history of hepatitis should never be used as donors for blood transfusion,[7] while individuals who have been intimately exposed to the disease should not be used as donors for at least six months. Such blood may be used for preparing plasma or plasma fractions, where adequate means for destroying the virus are used. When fresh, frozen, or freeze-dried plasma is needed, this should preferably be prepared from blood from a single individual, unless pooling is unavoidable. Thus, at the present stage of knowledge, homologous serum hepatitis is a calculated risk which the patient assumes as part of a blood or plasma transfusion.

7. Unfortunately, dangerous carriers of the hepatitis virus exist who give no history of hepatitis. (Oliphant, J. W.; Murray, R., and Neefe, J.: to be published; Stokes, J., Jr., and others; to be published.)

Syphilis.—Transmission of syphilis by transfusion is rarely heard of any longer. This is mainly due to the development of more sensitive tests for the detection of the disease in prospective donors, while another effective factor in preventing transmission of the disease is the widespread use of bank blood. Since the agent of this disease cannot live more than a few days outside the body, even at refrigerator temperature, the danger of transmitting syphilis is virtually nonexistent when blood or plasma aged for at least three days is used for transfusions. No individual with positive serologic tests for syphilis or a positive history of the disease should be used as a donor for fresh whole blood. In emergencies, when the necessary serologic tests cannot be carried out, a note to that effect should be entered on the patient's chart in order to protect the physician.

Malaria.—Transmission of malaria by transfusion is a difficult problem in regions where the disease is endemic, but until recently was not an important problem in the United States. It is a possibility which one must bear in mind now that there are so many veterans of World War II and Korea who have returned from regions where malaria is endemic, and who have become prospective blood donors. Instances have been observed where malaria (notably Plasmodium malariae) was transmitted by blood donors who had had the disease more than 30 years previously. For obtaining fresh blood for transfusion, individuals who have had malaria or who have received suppressive therapy for malaria while residing in a malarious region should not be used as donors for a period of at least two years following the last proved attack or discontinuance of suppressive therapy.[8] Obviously, malaria cannot be transmitted by plasma which is free of cells. The P. malariae can survive in the refrigerator for as long as five days, so that bank blood less than five days old may be infectious. In regions where malaria is endemic, so that the use of donors who have had the disease is unavoidable, one can take advantage of the fact that the plasmodium dies after prolonged storage. In unusual emergencies, where possible malarial carriers must be used as donors for fresh blood transfusions, antimalarial therapy should be given to the recipient.

Other Infectious Diseases.—Other infectious diseases such as measles and influenza have been transmitted by blood transfusion. This has occurred when the donor was in the prodromal stage of the disease when his blood was used for transfusion. Needless to say, all prospective donors should be examined in order to detect the presence of infectious disease. In emergencies where no other donor is available, donors with mild upper respiratory infections may be used. Mild chronic infections such as sinusitis, mild acne, and mild pyorrhea generally are not considered sufficient to exclude an individual from being a blood donor. No absolute set of rules can be drawn up to cover every conceivable situation with which the examining physician may be confronted, and the physician is therefore expected to use his best judgment before deciding to use any individual as a blood donor.

Contaminated Blood.—A difficult problem which has arisen as a result of the widespread adoption of bank blood is the danger of transfusing contaminated blood. Reports have appeared in the literature from time to time of deaths following such transfusions, and this is one of the most serious limitations to the use of stored blood.[9]

When fresh citrated blood was used exclusively for transfusion, open techniques for collecting the blood were prevalent, and it was only the introduction of blood banks that made the adoption of closed techniques imperative. As blood and plasma age they may lose their bacteriostatic and bactericidal properties due to the loss of complement and leukocytes, and aged plasma or blood is an excellent culture medium for bacteria. When blood is collected, even using the most rigorous aseptic techniques, it is unavoidable that occasionally some bacteria will be picked up from the deeper layers of the skin. Some of these organisms die or at least are prevented from multiplying

while the blood is still fresh, and the low temperature at which blood is stored will tend to prevent the growth of the majority of bacterial contaminants later on. Unfortunately there are some bacteria which multiply readily at refrigerator temperature,[10] and whose presence may not be detected because they fail to hemolyze blood. The bacteria that have heavily contaminated blood, transfusion of which has been followed by shock and death [11] generally have been either of the genus Pseudomonas or of the coli-aerogenes group. In the latter group Escherichia freundii and Paracolobactrum aerogenoides appear to be the most important.[10]

Bacteriological surveys [12] have shown that as many as 5 to 10% of specimens of bank blood are contaminated with bacteria. Most transfusions of such blood cause no harm because the majority of the micro-organisms present are gram-positive bacteria which are relatively low in pyrogenicity, do not grow at refrigerator temperature, and are generally nonpathogenic. Routine bacteriological control of bank blood is not practicable, because the blood will age further while the cultures are being made, and the very act of obtaining a specimen of blood for the bacteriological examination may serve to contaminate the blood. Various antiseptics and antibiotics have been tried to inhibit the growth of bacteria in stored blood and plasma, but nontoxic quantities of such chemicals have proved ineffectual for checking the growth of bacteria.[13] At the present time it is not considered advisable to add any antiseptic to blood in an attempt to prevent bacterial growth, and prime reliance must be placed on stringent aseptic technique when collecting and storing the blood.

According to the requirements of the National Institutes of Health, it is not permissible to enter a bottle of bank blood to obtain a sample at any time before the blood is to be administered. The obvious purpose of this rule is to avoid contaminating the blood. Therefore, the grouping and cross-matching tests are generally carried out with the sample of blood in the pilot tube. However, there is no real objection to entering the bottle itself, provided the blood is to be administered no more than a few hours thereafter. If the bottle of blood is entered and the blood is not transfused immediately, it should not subsequently be used for transfusion as whole blood. A competent worker should inspect every bottle of blood in the blood bank daily for evidence of hemolysis, which can be detected as a zone of hemoglobin diffusing upward from the layer of sedimented cells. In rare cases of doubt, a sample of blood may be drawn from the bottle, inverted, and centrifuged, and then any hemolysis which may have occurred will be plainly visible as a discoloration of the supernatant plasma.

Summarizing, the problem of bacterial contamination when stored blood is used for transfusion has not been completely solved at the present time. The use of closed aseptic techniques for collecting blood and careful control of the temperature during storage reduce the chance of contamination and bacterial multiplication. Despite impeccable technique a certain amount of contamination is inevitable. In order to limit the growth of bacteria, the period of storage of blood should be made as short as possible and certainly not permitted to exceed three weeks, in conformity with the requirements of the National Institutes of Health. The addition of bactericidal or bacteriostatic chemicals to stored blood is not recommended.

OTHER ACCIDENTS FOLLOWING TRANSFUSION

Embolism.—During storage of blood or plasma, precipitation of fibrin gradually occurs, and if such blood or plasma is transfused unfiltered, multiple embolization into the lung bed may occur, or, if the recipient has a cardiac septal defect, into the viscera or brain. The older literature contains reports of sudden death following transfusions of such unfiltered plasma or blood, which probably can be explained on this basis. Therefore, bank blood and stored plasma should always be filtered during transfusion, and in fact commercial transfusion apparatus are available which have suitable filters in the drip chamber for this purpose.

Rapid transfusion of blood by pumping air under pressure into the blood reservoir has caused a number of deaths from air embolism. Such accidents are inevitable when this method is used, unless a qualified transfusionist is constantly in attendance and vigilant during the procedure, in order to terminate it before air has a chance to enter the vein. Since the method is not foolproof, transfusion of blood under air pressure is to be condemned. If blood must be transfused rapidly, it is a simple matter to insert a two way stopcock between the needle in the patient's vein and the infusion tubing, and to pump the blood in by syringe. The rate of the flow can also be increased by inserting a larger needle into the vein and raising the blood reservoir, or by setting up multiple blood infusions into both arms and legs of the recipient. The collection of blood in plastic bags also makes possible rapid administration under pressure without the danger of air embolism. The transfusionist must bear in mind that air embolism as the cause of a recipient's death may be considered prima facie evidence of negligence.

The local injury produced by the needle in the patient's vein may cause a thrombophlebitis with secondary embolism. Since the chance of phlebitis developing is directly related to the length of time the needle remains in the vein, the infusion should not be unnecessarily prolonged. Moreover, transfusion by improving the patient's circulation may be indirectly responsible for embolism from the site of an operation or an occult phlebothrombosis in the veins of the calves of bedridden patients. The rare accidents of this type are hardly ever predictable.

Thrombophlebitis.—Transfusions are given by entering an accessible vein through the skin with a suitable intravenous needle. At the termination of the transfusion the needle is withdrawn and a sterile compress applied to the puncture site, and only very rarely does any local infection or thrombosis of the vein result. Should blood infiltrate the tissues around the vein, it is usually absorbed without any serious local reaction. In emergencies, when the patient is in collapse from hemorrhage, it may be necessary to cut down on a vein and there may not be enough time to take complete aseptic precautions. In such situations, local infection and thrombophlebitis may result, and therefore adequate doses of an appropriate antibiotic or chemotherapeutic agent should be administered prophylactically.

Allergic Reactions.—About 1% of blood transfusions are followed by reactions of an allergic type. As a rule these reactions are mild and consist merely of the appearance of urticaria. Such a mild reaction does not make necessary the interruption of the blood transfusion, and if the itching is troublesome, 2 or 3 minims of 1:1,000 epinephrine may be administered subcutaneously. Angioneurotic edema is a more serious allergic manifestation which may be dangerous if it involves the larynx. Rarely, the recipient may exhibit asthmatic breathing after a transfusion. Should any recipient begin to wheeze or exhibit signs of angioneurotic edema, the transfusion must be discontinued at once, and small doses of epinephrine administered until the symptoms abate.

Allergic manifestations may be due to the presence in the donor's plasma of some food protein or drug to which the recipient is sensitized. Therefore, whenever possible only fasting donors should be used for blood transfusions to allergic recipients or for the preparation of blood plasma. On the other

10. Pittman, M.: Psychrophilic and Other Bacterial Contaminants from Human Blood and Plasma, read at the Proceedings of the Fifth Annual Meeting of the American Association of Blood Banks, Milwaukee, Oct. 9-11, 1952.

11. Borden, C. W., and Hall, W. H.: Fatal Transfusion Reactions from Massive Bacterial Contamination of Blood, New England J. Med. **245**: 760-765 (Nov. 15) 1951.

12. Braude, A. I.; Sanford, J. P.; Bartlett, J. E., and Mallery, O. T., Jr.: Effects and Clinical Significance of Bacterial Contaminants in Transfused Blood, J. Lab. & Clin. Med. **39**: 902-916 (June) 1952.

13. Swedberg, B.; Widström, G., and Alin, K.: Importance of Aseptic Technique and Fallaciousness of Chemical Bacteriostatics in Blood Banking and Plasma Preserving, Acta med. Scandinav. **127**: 480-493, 1947.

hand, inverse allergic reactions may result from the passive transfer of reagins from donor to patient. Such reactions may be immediate if the corresponding antigen is present in the recipient's body, or it may be delayed for days, depending on the next exposure to the antigen. Therefore, it is best not to use allergic individuals as blood donors. When no other donors are available, however, individuals with seasonal hay fever may be used at times of the year when the pollen to which they are sensitized is not prevalent.

Patients receiving repeated blood transfusions occasionally become sensitized to some ingredient of the plasma, and then exhibit chills and fever with each transfusion. By giving such individuals merely the washed red blood cells of the donor the chance of such reactions is reduced. Occasionally allergic reactions have been traced to sensitivity to some constituent of rubber tubing.‖ They are avoided by using plastic tubing.

Summarizing, allergic reactions following transfusion are hardly ever serious, and the occurrence of such reactions after approximately 1% of transfusions is to be expected. As a rule, allergic reactions do not interfere with the transfusion.

Pyrogenic Reactions.—In the past pyrogenic reactions were not only a nuisance, but in severely debilitated patients occasionally precipitated death from cardiac failure. The cause of such reactions has been traced to the growth of bacteria in the water used for preparing solutions, or in moisture adherent to the apparatus, before they are sterilized. Methods have been developed for preparing pyrogen-free solutions and apparatus, which are readily available commercially. Accordingly, pyrogenic reactions are no longer an important problem, and one should not accept such reactions as inevitable after intravenous infusions.

Overloading.—Too rapid transfusion or the transfusion of too much blood may cause deaths from congestive cardiac failure or cerebral hemorrhage. At one time, when it was customary to transfuse unmodified blood by syringe-valve apparatus, it was necessary to pump the blood in rapidly in order to avoid coagulation in the transfusion apparatus. By this technique occasionally distention of the neck veins was present at the termination of the transfusion, and certain instances of sudden death following transfusion were undoubtedly due to the too rapid injection of blood. The demonstration that sodium citrate is an innocuous anticoagulant converted transfusion from a spectacular procedure into a simple one deliberately performed, and increased its safety for the recipient. Unfortunately, a certain number of deaths from too rapid transfusion still occur, especially when transfusions are given to infants. Because of the technical difficulty of transfusing infants, there is a tendency to give too much blood and too rapidly. The danger of transfusing infants will be considerably reduced if this procedure is carried out only by experienced transfusionists, who are familiar with the problem of dosage and rate of transfusion.

Citrate Reactions.—The sodium citrate which is introduced during transfusion is rapidly metabolized and excreted. Therefore, the amount of citrate administered with 500 cc. of blood is harmless to the adult. However, when massive transfusions are given in a short period of time sodium citrate may accumulate in the blood stream, so that signs of hypocalcemia may result, namely, a drop in blood pressure and tetany. This possibility should be borne in mind when adults with massive hemorrhage require more than a liter of blood. If the practice is followed to inject slowly into the recipient's vein 10 cc. of a 10% solution of calcium gluconate after every 1,000 cc. of citrated blood, hypocalcemia can be prevented. Similarly when performing exchange transfusions on erythroblastotic babies, some transfusionists inject 1 cc. of 10% calcium gluconate after every 100 cc. of citrated blood; others meet the problem by removing part of the citrated plasma from the blood to be used for the transfusion.

Intra-Arterial Transfusion.—For obvious reasons, transfusions are almost invariably given into one of the veins. From time to time, the use of the intra-arterial route has been proposed for blood transfusion. Recently intra-arterial transfusion has again been advocated particularly for patients in deep shock from hemorrhage, who have failed to respond to intravenous transfusions. Such emergencies arise occasionally in the operating room after massive hemorrhages, such as may occur in the course of an operation on the lungs or heart. It has been claimed that introduction of blood into the circulation through an artery (usually the radial artery is used) under pressure causes the blood to enter the aorta directly, thus producing an immediate rise in blood pressure. Actually, the published experimental and clinical observations on intra-arterial transfusion have not supported its supposed theoretical advantages.[14] In addition, the method has the disadvantage that it is necessary to cut down on an artery, and after the transfusion the artery may thrombose and gangrene result. In view of the debatable status of the procedure, intra-arterial transfusions must still be considered an experimental procedure to be resorted to only in unusual cases of emergency.

Intramedullary Transfusion.—Many investigations have been carried out on the use of the intramedullary route for infusions, and numerous blood and plasma transfusions have been given successfully through the bone marrow. In adults generally the infusion is given through the sternal marrow, while in infants and small children where the sternum is too thin the tibial route is used. In general, the intramedullary route for ordinary transfusions is not recommended because of the danger of fat embolism, and, especially in children, the procedure has resulted in osteomyelitis and fractures of the tibia. The need for the intramedullary route in pediatric practice is avoided when trained individuals are available, who are skilled at intravenous procedures. In infants, scalp veins are generally available, and surprisingly large veins can frequently be found on the back of the hand, in the bend of the elbow, or at the ankle. If necessary, a cutdown can be carried out, and a vein can always be found anterior and superior to the medial malleolus at the ankle. Intramedullary transfusion has its main application in instances of extensive burns or patients with skin diseases which make intravenous therapy difficult. In such cases, the intramedullary routes offer a ready solution, and the method has proved particularly valuable in civilian catastrophies and in military medicine.

Other Routes.—Transfusion into the longitudinal sinus is dangerous because of the possibility that blood may be injected extradurally. Nobody any longer advocates the use of the intraperitoneal or penile routes.

PROTECTION OF THE BLOOD DONOR

At one time it was difficult to convince individuals to donate their blood for transfusion purposes. Experience during World War II has educated the public regarding blood transfusion, and demonstrated the relative harmlessness of being a blood donor. By the time the Red Cross Program was completed at the end of World War II as many as 13 million pints of blood had been donated,[15] and at the present time blood continues to be collected for civilian and military purposes at the rate of millions of pints per year. However, if adequate precautions are not taken to safeguard the welfare of the blood donor, his health may be jeopardized or even his life.

Secondary Anemia.—The most obvious danger of repeated blood donations is the development of secondary anemia. This danger is greater for women because of their smaller body size and blood volume, and because in addition they are subjected to periodic physiological blood losses. Therefore, women should donate blood at less frequent intervals than men. It is now a general policy not to permit donors to donate a pint of blood oftener than every 10 to 13 weeks, or until such time as the blood attains a hemoglobin concentration of at least 12.5 gm. per 100 cc.; or a specific gravity of 1.053 or higher. When donors take iron by mouth blood regeneration occurs more rapidly.

In this connection, the needle used for puncturing the finger to obtain blood for the hemoglobin concentration should be sterile in order to avoid the possibility of transmitting the hepatitis virus. Either individual expendable lancets should be used for this purpose, or individual lancets which have been

‖ New rubber tubing must be specially treated in order to avoid toxic reactions of a nonspecific nature.

15. American Red Cross Blood Donor Service During World War II: Its Organization and Operation: ARC 1267, Washington, D. C., American National Red Cross, 1946.

subjected to sterilization procedures which have been shown to be capable of destroying the virus. Merely wiping the lancet with alcohol or immersing it in an antiseptic solution is not adequate. Sterilization for a sufficient length of time by dry heat, boiling or autoclaving will destroy the hepatitis virus.

Fainting.—The most disturbing accident occurring after a blood donation is faintness, or actual fainting, and occasionally deep unconsciousness. In this emotional factors play a certain role, because in some cases donors have fainted before they were bled, or the wife or husband fainted when the other marital partner was bled. Aside from the psychic aspect, the precipitating cause of fainting is the sudden reduction in blood volume. The incidence of fainting has been reported as varying between 1 and 6%; some persons are more predisposed to faint than others, and there is also a greater tendency to faint among donors of smaller size and lower blood volume. To counteract this tendency some transfusionists make a practice of taking smaller amounts of blood from such donors.

Probably one of the most important precautions is the proper care of the donor before the donation. The incidence of fainting can be reduced by screening out unsuitable donors by physical examination in order to exclude those with low blood pressure or a low hemoglobin level, or with small body size. Experience of blood banks shows that it is necessary to reject 10 to 15 times as many female donors as male donors. According to certain workers, when great care is taken to screen donors, the percentage of rejections may be as high as 28%.

A donor who has been without food for a long time or who makes his donation after coming off a night shift may be a candidate for fainting. Under these circumstances, a light snack immediately before drawing the blood will not spoil the plasma and may help to prevent unpleasant reactions. After the donation the donor should be kept in a supine position until he has apparently recovered. The nervous donor should be made to feel at home, and his attention should be diverted from the procedure by conversation about pleasant matters. The bleeding room should be light and airy, and smoking should not be permitted in it or in the resuscitation room. It has been demonstrated that the fainting rate can be reduced in donors from hot work-shops if they drink some isotonic sodium chloride solution before the bleeding, and certainly on hot days a glassful of water is a beneficial preparatory measure. If fainting or loss of consciousness should occur, it is handled by holding the head low, loosening the clothes and providing fresh air. Occasionally, intravenous infusions of sodium chloride solution may be required, and in very rare instances the donor's own blood may have to be restored to him. If it appears advisable, the donor may be kept in the hospital overnight. When such a donor has fully recovered it may be wise to send him home by car or with an escort.

More serious than fainting immediately after the donation is the occasional occurrence of syncope after the donor has left the hospital. The donor may fall and lacerate his scalp or even fracture his skull, or if he falls in the street in the midst of traffic or at work in a factory he may become involved in a serious accident. Therefore, donors involved in hazardous occupations should be advised not to return to work for at least 12 hours.

Thrombosis and Infections.—Needless to say stringent precautions must be taken to prevent infection of the puncture in the donor's arm. Although a certain percentage of hematomas is inevitable, especially when difficulty is encountered in entering the vein, such hematomas almost invariably disappear without sequelae. In very rare instances, thrombophlebitis or abscess formation has occurred at the site of the puncture, and at least one lawsuit against a blood bank has resulted. While the tendency of the court has been to favor the blood bank, provided there was no evidence of negligence in the performance of the phlebotomy or in the aftercare of the donor, it is wise for the blood bank and physician to protect themselves by suitable insurance.

In conclusion, one may state that the donation of a pint of blood by a healthy adult is safe. Among the 13 million donations during the war, there was only a single reported fatality caused by a sudden attack of coronary occlusion, and 10 additional fatal cardiovascular accidents which occurred 3 to 48 hours after the donor left for home. These few severe cardiovascular accidents are certainly no more frequent in number than would be expected among several million persons no matter what they did before death.

PREPARATION OF BLOOD DIAGNOSTIC SERUMS

Reliable blood grouping tests are possible only when potent and specific diagnostic serums are available. Therefore, the preparation of blood diagnostic serums is an essential aspect of the practice of blood transfusion. At one time anti-A and anti-B serums were obtained from random group B and group A individuals, respectively; similarly, anti-Rh serums were procured from Rh-negative individuals accidentally sensitized by blood transfusion or pregnancy. However, such antiserums selected at random are frequently of low titer and avidity, so that the use of such reagents has caused errors in blood grouping. Potent and specific antiserums can be obtained most consistently by deliberate immunization. For this purpose, experimental animals have yielded unsatisfactory results, so that human subjects have to be used for the preparation of diagnostic serums.

Immunizing and bleeding donors for the purpose of preparing blood diagnostic serums carries no hazard other than those associated with the blood donation and transfusion. In fact, though thousands of individuals have been immunized and bled for this purpose to date, no harmful effects from the procedure have ever been reported. At least one insurance company has permitted physicians of New York City doing this essential type of work to have a rider placed on their malpractice insurance policies to protect them against possible claims. While it has not been necessary to take advantage of this rider so far the practice should be adopted throughout the country in order to encourage the preparation of potent serums essential for safe transfusion practice.

Men are used more often than women for the preparation of diagnostic serums. Obviously no Rh-negative woman should be immunized with Rh-positive blood to prepare anti-Rh serums if there is any chance of her becoming pregnant later on. Similarly immunization of a group A woman against agglutinogen B or vice versa could conceivably cause obstetric complications. This limitation does not apply, of course, to women who are not capable of bearing children.

While the commoner serums, anti-A, anti-B, and anti-Rh_o, can be prepared by deliberate immunization of male volunteers, this technique is not readily applicable to weaker antigens such as rh′, rh″, hr′, hr″, Kell, and Duffy. To obtain these rarer reagents, one must depend principally on unusual clinical cases of erythroblastosis or hemolytic transfusion reactions caused by sensitization to these blood factors. The cooperation of physicians treating such patients, whether male or female, is therefore needed, so that some of their blood can be obtained for the preparation of diagnostic serums. Large amounts of blood may be withdrawn even from anemic individuals, provided that it is replaced by transfusions of carefully selected blood.

For preparing anti-A and anti-B serums, a number of different immunization procedures have been used successfully. The intravenous injection of blood group substances prepared from horse and pig stomach carries the possibility of anaphylactoid reactions in allergic subjects. This danger is avoided by using deproteinized preparations, such as are commercially available, and by administering them intramuscularly instead of intravenously. No serious reaction has been observed following such injections. For the preparation of anti-Rh serums, human blood must be injected intravenously; some workers use human blood also to prepare anti-A and anti-B serums. Because of the small volume of blood injected, the amount of intravascular hemolysis is negligible. Nevertheless, some subjects have complained of pain along the course of the vein during the injection, or have had a mild rise in temperature later on. The former can be avoided by diluting the blood with sodium chloride and injecting it more slowly; the latter by having the donor take 5 grains (0.32 gm.) of acetylsalicylic acid at the time of the injection or by reducing the dosage. Any injection of human blood carries with it the theoretical danger of homologous serum hepatitis. Against this eventuality

the same precautions should be taken as with the selection of a donor for blood transfusion.

Needless to state, before injecting blood or blood group substances into any volunteer, one must explain the purpose of the injection to him and make a full disclosure of the facts. At the same time one should point out the harmlessness of the injections as far as the subject's health is concerned. The sensitized Rh-negative donor could be given a suitable identification card, and warned that only Rh-negative blood be used for any transfusion he may require in the future, e. g., after an accident or operation. A signed release should be obtained from the donor, although such a release may not in all cases constitute a bar to a lawsuit.

In a few instances, volunteers immunized against the Rh factor have developed antibodies against other antigens, most frequently agglutinogen M. This can be avoided by testing all subjects for the M-N types, and using only type N, Rh-positive blood for Rh-negative donors of type N. Should sensitization to agglutinogen M as well as Rh occur, this is no serious matter, and if for subsequent injections only type N blood is used, the immune anti-M agglutinins soon disappear. Should an exchange transfusion be undertaken on such a subject, the antibodies for M as well as Rh must be taken into account in order to avoid a hemolytic reaction. As an additional precaution, exchange transfusion on immunized donors might be preceded by a biological test, namely a test injection of a small amount of the blood to be used for the transfusion.

Summarizing, human subjects are necessary for the preparation of high quality diagnostic serums essential for safe blood transfusion practice. The same high standards applied to ordinary blood donors and recipients should be used when handling such volunteers. Physicians are urged to enlist the cooperation of patients whose plasma contains rare blood group antibodies, so that their blood can be used for the preparation of diagnostic serums. Insurance companies specializing in malpractice insurance can aid the work by providing riders on policies of physicians specializing in this field.

QUALIFICATIONS OF TRANSFUSIONISTS

The administration of blood and plasma nowadays is mostly delegated to residents or physicians not specializing in this field. In general, such physicians are fully qualified to carry out blood or plasma transfusions, which in the average case offer no unusual difficulty. Situations arise, however, in which transfusions can be performed only by specially trained physicians, namely, on patients in deep shock with collapsed veins, and infants and children or other individuals with poorly developed veins. In addition, problems arise when atypical results are obtained in the blood grouping and cross-matching tests, or when reactions occur after transfusions of apparently compatible blood. Therefore, every hospital should have one or more qualified individuals responsible for the transfusions performed there. These specially qualified physicians should have the responsibility to see that the residents are properly trained to perform transfusions, and should be available to advise and assist them when problems of unusual difficulty arise. Obviously, highly technical procedures, such as an exchange transfusion, a superior longitudinal sinus transfusion, or intra-arterial transfusions, should not be undertaken except by specially trained physicians, or under the direct supervision of such individuals.

The withdrawal of blood offers fewer technical difficulties than its administration. Therefore, in many blood banks specially trained nurses or technicians are permitted to bleed donors. Wherever this is done it should be under the direct supervision of a qualified physician.

RECOMMENDATIONS

This report summarizes the present status of knowledge concerning the dangers of blood and plasma transfusion. The various untoward sequelae which may follow such transfusions and the precautions that can be taken to prevent them have been discussed in detail. It is recommended that the report be distributed to all individuals concerned with blood and plasma transfusion, in order to increase further the safety of this important therapeutic procedure.

¶ Prepared by the Bureau of Legal Medicine and Legislation, January, 1953.

ADDENDUM ¶

COURT DECISIONS

Necolayff v. Genesee Hospital, 61 N.Y.S. (2d) 832 (New York, 1946), J. A. M. A. **132:**810 (Nov. 30) 1946.—Here a hospital was sued by a patient for damages for injury which resulted because she had been given a blood transfusion in error. Patient alleged she suffered chills and a severe headache following the transfusion and later became mentally ill, spending some time in a state hospital for the insane. At the time of the transfusion patient was at or approaching her menopause and the transfusion was the turning point that caused her illness. Evidence established that a nurse and an intern, on proper order to transfuse a patient other than the plaintiff, through mistake entered plaintiff's room and commenced to administer a transfusion to her over her protest. The hospital disclaimed liability on the ground that it was a charitable hospital, although plaintiff was not a charity patient. The Supreme Court of New York, appellate division, held the hospital responsible for the negligence of its nurse and intern on the ground that the hospital, through its employees, was obligated to safeguard its patients. The nurse and intern by their negligence in entering the wrong room and transfusing the wrong patient failed to perform an administrative duty and their negligence is attributable to the hospital. Not having administered the transfusion to the proper patient the nurse's and intern's act, said the court, could not be considered a professional act.

Mississippi Baptist Hospital v. Holmes, 55 So. (2d) 142 (Mississippi, 1951), J. A. M. A. **150:**1336 (Nov. 29) 1952.—In this case a hospital was sued for the death of a patient who died as a result of having been transfused with blood of the wrong type. Evidence disclosed that a hospital laboratory technician, on proper orders, took blood samples from the deceased and another patient for the purpose of determining blood types for transfusion purposes. The types were properly ascertained by the technician as type 4 for the deceased and type 2 for the other patient, but in preparing the blood to be used for each patient the technician reversed the labels. Deceased, during surgery, was transfused with type 2 blood and death ensued as the result of acute hemolytic anemia. The hospital claimed it was not liable for its technician's negligence because it was a charitable hospital even though deceased was not a charity patient. The Supreme Court of Mississippi held the hospital liable saying that a charitable hospital should be held liable for the negligent act of its employee that proximately caused the death of the deceased to the same extent as it would had it failed to exercise reasonable care in the selection, employment, and retention of the employee. The court specifically denied that charitable hospitals enjoy immunity from liability in Mississippi solely because of their charitable character.

Parker v. State, 105 N.Y.S. (2d) 735 (New York, 1951), J. A. M. A. **148:**1359 (April 12) 1952.—Representatives of the deceased sued the state for damages resulting from death following a transfusion of pooled blood plasma infected with homologous serum jaundice. Evidence disclosed that deceased, found unattended in a critical condition, had been taken to a hospital and there, incident to shock therapy, was given a tranfusion of pooled blood plasma. Later that individual died of hepatitis, and evidence was clear that death resulted from the fact that the plasma used (war surplus blood plasma originally procured by the Red Cross for the armed forces and recently distributed to the several states through appropriate agencies) had been infected with the jaundice virus. The essence of plaintiff's action was that the state was negligent in distributing this plasma and in failing to warn of the danger of its use. The court of claims reviewed the history of blood plasma, its use, and dangers incident to its use, finding that medical experience and knowledge rendered the administration of blood or blood derivatives a recognized therapeutic device which is used in the presence of established clinical symptoms. The court also found that it is a matter of medical judgment to determine in a particular case whether to administer plasma immediately despite the danger of serum jaundice or to risk the danger of delay involved while awaiting safer whole blood properly selected or O blood treated with Witebsky's solution. The court held therefore that the state was

not negligent in distributing the plasma (a therapeutic device) or in failing to advise physicians and hospitals concerning its use (a professional decision).

National Homeopathic Hospital v. Phillips, 181 F. (2d) 293 (1950), J. A. M. A. **144:**202 (Sept. 9) 1950.—Here a hospital was sued for damages for the death of a patient following a transfusion of incompatible blood which had erroneously been tested and reported as compatible by a hospital technician. The question before the U. S. Circuit Court of Appeals was whether there was such a relationship between the hospital and the technician as to make the hospital liable for the technician's negligent act. Evidence disclosed that the hospital ordered the test to be made, that it was made by a technician hired and paid by the hospital, and that the hospital caused the transfusion to be administered in reliance on the technician's report. The test although conducted in a laboratory which was an established part of the hospital and operated under the over-all supervision of an outside physician was not made in the presence or under the supervision of the physician. The court held that a master-servant relationship did exist between the hospital and the technician and clearly established the responsibility of the hospital for the technician's negligence. The court added that this responsibility is unaffected even though a statute requires that technical work in a laboratory be put under the direction of a physician.

Brown et ux. v. Shannon West Texas Memorial Hospital, 222 S.W. (2d) 248 (Texas, 1949), J. A. M. A. **141:**1077 (Dec. 10) 1949.—Plaintiff sued the hospital and Baylor University for damages for an infection in her arm alleged to have been incurred when she donated blood in response to a request from the hospital. Plaintiff claimed the hospital was liable because it furnished a nonsterile needle to be used in withdrawing blood and the University was liable for having furnished the hospital with a contaminated needle. Evidence disclosed that under an arrangement with the University the hospital collected blood and sent it to the University for processing and return, using "collecting units" furnished by the University. These units, consisting of towels, tubing, hypodermics for local anesthesia, and needles, were sterilized and packed at the University, sent to the hospital, and there used without resterilization. While it was not disputed that plaintiff had had an infection following the procedure, her own physician testified there was no way to determine when the infection was introduced and another physician testified that the source of an infection could not be ascertained in the absence of a culture. Blood received at the University at the time in question was not contaminated. The court of civil appeals, finding that no medical expert fixed the source of the infection, said plaintiff did no more than show that her injury could have resulted from the use of a nonsterile needle. Because the plaintiff failed to prove that an infected needle was used and that the infected needle was the proximate cause of the injury judgment in favor of the hospital and University was affirmed.

Giambozi v. Peters, 16 A. (2d) 833 (Connecticut, 1940), J. A. M. A. **117:**2192 (Dec. 20) 1941.—In this case a physician was sued by representatives of a deceased patient for breach of contract to cure, for malpractice which caused a disease, and for negligence causing death. Evidence disclosed that after patient gave birth to a child her then attending physician summoned defendant to give her a transfusion. This the defendant did, using the blood of a volunteer without making a test for syphilis. Later patient having learned she had a syphilitic infection allegedly incurred as a result of the transfusion went to defendant for treatment. (He, it was alleged, agreed to effect a cure.) During treatment patient died following an injection of neoarsphenamine. The Supreme Court of Errors of Connecticut said the complaint asserted three distinct bases for recovery and held that a different statute of limitation applied to each one: for breach of contract the statute commenced at the time the contract was broken, or at death in this case; for malpractice the statute commenced when the negligent act or omission (failure to test for syphilis) occurred; and for negligence (negligence in treatment for infection) when it occurred. The court held that the action against the physician for negligence and for malpractice was barred by these statutes but that further proceedings should be held on the question of breach of contract.

MEDICAL MOTION PICTURES

Testing and Individual Therapy for Aphasic Patients: 16 mm., color, sound, showing time 28 minutes. Produced in 1950 for the Veterans Administration by Churchill-Wexler Productions, Los Angeles. Procurable on loan from VA Central Office Film Library, Motion Picture Service, Office of Information, U. S. Department of Agriculture, Washington 25.

This is the second in a series of motion pictures on aphasia. The film deals with examining procedures as well as therapy. Covering as much material as was attempted to cover in this film resulted in hitting only the high points without presenting enough detail on any one point to make the film particularly useful to students. The examination procedures demonstrated were first, neurological, second, electroencephalographic, and third, psychological, which probably results only in a small sampling of their complete testing technique. The language therapy program is very well done. There was emphasis on kinesthetic controls and training in "The Speech Act." This may be simply the result of the sampling training techniques rather than representing the particular bias on therapy.

There was an implication that certain skills were established first and contacts with other persons were second in sequence. Many therapists would reverse this order in training. The qualitative details of the film are invaluable; the stress on ideal testing conditions, the physical conditions and equipment for training, and the importance of personality and morale are all subtly presented. All in all, it is an excellent job, although some points might be controversial. The photography and narration are very well done. The film is worthy of very careful consideration by all persons who deal with aphasic patients. It would be most useful for psychologists, neurologists, and speech therapists.

Social Adjustment of the Aphasic Patient: 16 mm., color, sound, showing time 28 minutes. Produced in 1950 for the Veterans Administration by Churchill-Wexler Productions, Los Angeles. Procurable on loan from VA Central Office Film Library, Motion Picture Service, Office of Information, U. S. Department of Agriculture, Washington 25.

This is the third in a series of motion pictures on aphasia. The film shows a number of things that are important in rehabilitation work, such as group discussions of adjustment of attitudes, program in general education, occupational therapy, physical therapy, and vocational guidance. This is an excellent production. It does present a point of view for the organic basis, the examination, and training of aphasic cases. Whether or not workers in the field agree entirely with this point of view is immaterial. The most important thing is that this film represents very clearly the approach of a particular group of persons. Careful reporting of such points of view furnish a distinct contribution to scientific knowledge. The film will be of interest to psychologists and speech therapists.

NOTE: A review of the first film in this series entitled "Introduction to Aphasia" was published in THE JOURNAL, Nov. 24, 1951, page 1298.—ED.

Surgical Approaches to the Sternoclavicular and Acromioclavicular Joints: 16 mm., color, sound, showing time 19 minutes. Produced in 1952 for the Veterans Administration by Churchill-Wexler Productions, Los Angeles. Leroy C. Abbott, M.D., Technical Advisor. Procurable on loan from VA Central Office Film Library, Motion Picture Service, Office of Information, U. S. Department of Agriculture, Washington 25.

The discussion on the approaches to these two joints and the demonstration of every point of the anatomy are excellent and vivid. Having once seen the picture, one should have a clear idea as to what should be avoided and the ease with which these joints can be widely exposed. This is another product of the anatomy department of the University of California and lives up to the previous demonstrations in every way. This is a "must" for those interested in the subject illustrated. The picture is well organized, and the photography, animation, and narration are excellent. To the student, to the teacher of anatomy, and to the surgeon interested in the anatomy of the sternoclavicular and acromioclavicular joints, this film can be most heartily recommended.

MEDICAL LITERATURE ABSTRACTS

UNITED STATES

A.M.A. Arch. Internal Medicine, Chicago

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*Adrenocortical Function During Continuous Long-Term Therapy with Cortisone. E. P. Engleman, M. A. Krupp, H. P. Johnson Jr. and others. —p. 1.

Diagnostic and Therapeutic Value of Reproduction of Chest Pain. T. J. Reeves and T. R. Harrison.—p. 8.

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Varicella Pneumonia. S. Saslaw, J. A. Prior and B. K. Wiseman.—p. 35.

Bone Marrow Depression from Chloramphenicol. A. B. Ley.—p. 43.

*Histoplasma Capsulatum Infection Associated with Gastric Ulcer and Fatal Hemorrhage. T. J. Fitzpatrick and B. H. Neiman.—p. 49.

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Aureomycin, Chloramphenicol, and Oxytetracycline ("Terramycin") in Mumps. W. D. Sutliff and Z. B. Barnes.—p. 68.

Bronchiectasis: Bronchographic Study of 60 Cases of Pneumonia. A. L. Bachman, W. R. Hewitt and H. C. Beekley.—p. 78.

Kaposi's Sarcoma Associated with Lymphosarcoma. S. M. Bluefarb and J. R. Webster.—p. 97.

Parallel Relation of Hyperglycemia and Hyperlipemia (Esterified Fatty Acids) in Diabetes. E. F. Hirsch, B. P. Phibbs and L. Carbonaro. —p. 106.

Hypertension: Review of Significant Publications, July, 1950, to Jan. 1, 1952. R. W. Wilkins and P. Stucki.—p. 118.

Adrenocortical Function During Long-Term Cortisone Therapy.—In order to learn whether the suppression of adrenocortical activity that results from long-term treatment with cortisone is reversible, Engleman and associates studied the function of the adrenal cortex in 19 patients who were given so-called maintenance doses of cortisone for long periods. All patients had been treated with cortisone continuously for 12 to 26 months. The cortisone was administered orally and in daily doses ranging from 37.5 to 100 mg. Hospital patients who had not received cortisone served as controls. The study consisted of the administration of corticotropin until two of the following three criteria were satisfied: (1) a 60% or greater decrease in circulating eosinophils; (2) an increase of 50% or more in the 24-hour urinary excretion of 17-ketosteroids; and (3) an increase of 50% or more in the 24 hour urinary excretion of Porter-Silber chromogens (17, 21-hydroxy-20-ketosteroids), with a minimum rise of 0.5 mg. The maintenance oral doses of cortisone were continued throughout the test period. The results of studies made it apparent that the suppression of adrenocortical function that results from therapy with cortisone is reversible. Furthermore, each of five patients who were subjects of a similar study one year ago showed essentially the same responsiveness they demonstrated at that time. Thus there seems to be no need for interrupted courses of cortisone therapy or alternating courses of cortisone and corticotropin. The fact that most patients required repeated stimulation with corticotropin before adrenocortical response could be demonstrated shows that a dormant state of the adrenal cortex is often induced by cortisone. This emphasizes the need for constant alertness for situations of stress that may necessitate larger doses of cortisone, because of the inability of the pituitary-adrenal mechanism to respond spontaneously. Patients receiving cortisone therapy may require additional amounts during illness or after injury. Moreover, the delay in adrenal responsiveness to corticotropin during treatment with cortisone supports the clinical observation that sudden discontinuance of cortisone therapy is dangerous. Gradual reduction of the daily oral dose of cortisone allows the pituitary to resume secretion of endogenous corticotropin, which, in turn, results in recovery of adrenal function.

Gastric Ulcer and Fatal Hemorrhage During Histoplasma Capsulatum Infection.—A man, aged 63, was hospitalized on July 4, 1951, with a history of septic fever, chills, and night sweats for about two weeks. His temperature showed daily spikes to 102 or 103 F. He was given a course of pencillin and chloramphenicol (chloromycetin®). For the latter, oxytetracycline ("terramycin") was later substituted. He received one blood transfusion. The temperature spikes gradually became less, and he was discharged on July 26, 1951. Two weeks later he had to be readmitted because he continued to have septic fever. Repeated blood cultures showed no growth. Repeated examinations for malaria were negative. A week after admission edema of the ankles was noted, and the following day the patient expectorated bright red blood. With the appearance of tachypnea, cyanosis, and inspiratory basal rales, nasal administration of oxygen was started, and he was treated with mercurials and digitalis. In addition, he received penicillin and streptomycin. A course of chloroquine was given without obvious effect. The evening before his death he suddenly vomited about 500 cc. of bright red blood. Despite transfusions and supportive measures, he continued to vomit blood and passed red blood per rectum. He went into shock and died. On the basis of necropsy studies the anatomic diagnoses were (1) generalized disseminated infection with Histoplasma capsulatum, with involvement of the liver, lungs, spleen, and lymph nodes and (2) gastric ulcer associated with H. capsulatum infection with erosion of a blood vessel. Since the organisms were very prominent in the gastric ulcer, a possible causal relationship is suggested. Ulceration has been reported to occur commonly in the intestine of patients with histoplasmosis but never in the stomach. A study of the patient's family revealed that the incidence of histoplasmin and tuberculin skin reactivity and presence of pulmonary calcifications were no greater than would be normally expected of life-long residents of this geographical area.

Alabama State Medical Assn. Journal, Montgomery

22:171-194 (Jan.) 1953

Management of Congestive Heart Failure Refractory to Usual Treatment. J. T. Grimes.—p. 171.

Carcinoma of Colon Involving Abdominal Wall and Other Viscera. T. B. Hubbard Jr.—p. 174.

Surgical Management of Gastric and Duodenal Ulcers. F. W. Smith. —p. 177.

Ultrasonics in Osteoarthritis. F. F. Schwartz.—p. 182.

American Journal of Hygiene, Baltimore

57:1-124 (Jan.) 1953. **Partial Index**

Studies on Schistosomiasis Japonica in Formosa: III. Bionomics of Oncomelania Formosana, Molluscan Intermediate Host of Schistosoma Japonicum. S. Y. Li.—p. 30.

Characterization of Botulinal Hemagglutination. J. P. Lowenthal and C. Lamanna.—p. 46.

Complement Fixation with Three Types of Poliomyelitis Viruses Propagated in Tissue Culture. A. Svedmyr, J. F. Enders and A. Holloway. —p. 60.

Use of Penicillin and Sulfadiazine as Prophylactic Agents Against Streptococcal and Nonspecific Respiratory Infections Among Recruits at Naval Training Center. H. M. Gezon, J. S. Cook Jr., R. L. Magoffin and C. H. Miller.—p. 71.

Eradication of Blood-Induced Plasmodium Gallinaceum Infections in the Chick. J. Greenberg and G. R. Coatney.—p. 101.

Strain Differences in Plasmodium Gallinaceum Brumpt: V. Further Characteristics of BI Strain. E. M. Richeson, B. Highman, J. Greenberg and G. R. Coatney.—p. 114.

Periodicals on file in the Library of the American Medical Association may be borrowed by members of the Association or its student organization and by individual subscribers, provided they reside in continental United States or Canada. Requests for periodicals should be addressed "Library, American Medical Association." Periodical files cover only the last 11 years, and no photoduplication services are available. No charge is made to members, but the fee for other borrowers is 15 cents in stamps for each item. Only three periodicals may be borrowed at one time, and they must not be kept longer than five days. Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted.

American Journal of Medical Sciences, Philadelphia

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Cation Exchange Resin Therapy in Patients Receiving Cortisone or ACTH. L. Greenman, F. A. Weigand and T. S. Danowski.—p. 1.
*Anticoagulant Therapy in Acute Myocardial Infarction: Survey of Specialists' Opinions Concerning Indications, Results and Dangers. H. I. Russek and B. L. Zohman.—p. 8.
*Heparin in Treatment of Advanced Peripheral Atherosclerosis: Preliminary Report. H. Engelberg and T. B. Massell.—p. 14.
Study of Mural Thrombi on Myocardial Infarctions as Source of Embolization. S. Rubler and A. A. Angrist.—p. 20.
Evaluation of Amodiaquin (Camoquin) in Treatment of Relapsing Vivax Malaria. J. Love, R. Foulk, R. G. W. Williams Jr. and R. B. Mitchell. —p. 26.
Cause of Acute Pericarditis. R. L. Reeves.—p. 34.
*"Mercurial-Fastness" in Patients with Congestive Heart Failure: Correction of This State by Addition of Pyridoxine. S. Waldman and L. Pelner.—p. 39.
Mild Hemophilia: An Allelic Form of Disease. J. B. Graham, W. W. McLendon and K. M. Brinkhous.—p. 46.
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Treatment of Post-Pneumoencephalographic Headache with β-Pyridyl Carbinol Tartrate (Roniacol Tartrate). R. M. N. Crosby.—p. 61.
Electrolyte Abnormalities of Sweat in Fibrocystic Disease of Pancreas. R. C. Darling, P. A. DiSant'Agnese, G. A. Perera and D. H. Andersen. —p. 67.
Rheumatoid Arthritis Therapy: Rationale and Use of Chloroquine Diphosphate. G. G. Haydu.—p. 71.
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Acute Suppurative Bronchopneumonia. M. Ziskind and M. Saunders. —p. 81.
Some Recent Contributions in the Field of Geriatric Psychiatry. A. J. Silverman.—p. 101.

Anticoagulant Therapy in Acute Myocardial Infarction.—A questionnaire on the use of anticoagulant drugs in acute myocardial infarction was sent to several hundred internists and cardiologists in various medical centers throughout the United States. Of the 228 physicians who replied, 116 (50.9%) stated that they do not use anticoagulants routinely in the treatment of acute myocardial infarction. The clinical indications for the use of anticoagulant drugs as summarized by these physicians are previous myocardial infarction, congestive heart failure, the presence of a large infarct, profound or persistent shock, intractable pain, significant enlargement of the heart, previous thromboembolic phenomena, varicosities, previous or recent thrombophlebitis or phlebothrombosis, cardiac arrythmias, old age, debility, lethargy, obesity, diabetes, polycythemia, and any departure from a smooth or uneventful course. Most of the physicians who reported that they administer anticoagulants only when the clinical findings in a given case appear to favor the development of thromboembolism regard old age as an important indication for the use of these agents because elderly patients are more prone to thromboembolic complications. A smaller but significant number of physicians believe that anticoagulants should always be withheld in elderly patients because of the pronounced risk of serious hemorrhage. The fallacy in considering age a significant factor in the prognosis of the individual patient is emphasized by the authors. Among nonmedical factors influencing use of anticoagulants in this disease are the economic status of the patient, coercion by the patient's family or referring physician, the compelling influence of the wide publicity given to this therapeutic procedure, and the fear of criticism or even litigation for malpractice if such treatment is withheld. Serious hemorrhagic complications from anticoagulant therapy had been observed by 104 (45.6%) of the 228 physicians surveyed; 122 deaths caused by such complications were reported by 64 (28.1%) of the 228 physicians. All agreed that hospitalization and dependable laboratory facilities were necessary in every case in which anticoagulants were to be employed. As a result of these observations the authors state that, although anticoagulant therapy now occupies an important place in the management of acute myocardial infarction, neither the evidence to date nor the current method of usage by authorities in the field can support the concept that its routine employment is necessary or desirable.

Heparin in Advanced Peripheral Atherosclerosis.—A preliminary report is presented of the results of treatment with intermittent doses of heparin in 13 patients with obliterative atherosclerosis of the lower extremities. Heparin was given in doses of 100 mg. intravenously two or three times weekly for two to six months. In several cases it was administered daily for the first month. Digital plethysmographic recordings and level walking tolerance tests were made in 14 extremities. There was significantly improved digital blood flow in 8 of the 14 extremities. In eight extremities there was also a pronounced improvement in level walking tolerance after several months of heparin therapy. Clinically, 11 of the 13 patients had intermittent claudication and 9 of these improved symptomatically after one to several months of therapy. In discussing possible mechanisms of action of heparin in obliterative atherosclerosis, the authors state that reduction of large serum lipoprotein molecules to smaller ones always occurs following heparin administration. It is suggested that heparin as it clears lipemic serums probably also clears any liproprotein accumulation on the intimal surface. This might result in improved oxygen exchange through the capillary wall and is a possible explanation of relief of claudication following administration of heparin. Reduction of serum lipoproteins may affect walking ability also by increasing the possibility of healing of more recently developed atherosclerotic lesions. Although it is not yet possible to provide a definite explanation of the action of heparin in obliterative atherosclerosis, the authors feel that intermittent administration of heparin is a promising form of therapy for peripheral atherosclerosis.

"Mercurial-Fastness" in Patients with Congestive Heart Failure.—Ten patients between the ages of 51 and 68 with severe congestive heart failure and resistance to mercurial diuretics ("mercurial-fastness") were treated with intramuscular or intravenous injections of 2 cc. of meralluride (mercuhydrin®) sodium to which 100 mg. of pyridoxine is added. Satisfactory diuresis resulted from this combined treatment in all the patients. The danger of treatment with large doses of mercurials in the absence of a diuretic response is stressed. The mode of action of pyridoxine in breaking "mercurial-fastness" is unknown, but it is probably effective at an enzymatic level. Resistance to mercurial diuretics may become manifest in any combination mixture and necessitates changing from one to another to maintain successful diuresis.

American Journal of Psychotherapy, New York

6:673-856 (Oct.) 1952. **Partial Index**

Tentative Interpretation in Psychotherapy. A. H. Chapman.—p. 677.
Some Observations Upon Specificity in Psychosomatic Medicine. D. M. Lipshutz.—p. 683.
New Attempt in Psychotherapy with Juvenile Delinquents. A. E. Buck and T. Grygier.—p. 711.

Am. J. Roentgenol. & Rad. Therapy, Springfield, Ill.

69:1-178 (Jan.) 1953

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Intestinal Obstruction in Fibrocystic Disease of Pancreas. A. Bruwer and J. R. Hodgson.—p. 14.
Accessory Pancreatic Tissue in Stomach Wall. J. A. Evans and S. Weintraub.—p. 22.
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Transdiaphragmatic Duplication of Alimentary Tract. J. J. Snodgrass. —p. 42.
Volvulus of Stomach: Report of Case. D. L. Jenkinson and L. C. Bate. —p. 54.
*Roentgenographic Diagnosis of Tumors of Glomus Jugularis. P. A. Riemenschneider, G. D. Hoople, D. Brewer and others.—p. 59.
Hemangioma of Mediastinum: Case Report. J. M. Keegan.—p. 66.
Saccular Outpouching of Right Ventricle in Child Visualized by Angiocardiography. G. Miller, M. Lowenthal, S. Krause and P. Rosenblum. —p. 69.
Uterosalpingography: With Special Reference to Cervical Canal. T. M. Fullenlove.—p. 74.
Newer Radiopaque Media for Oral Cholecystography. W. G. Scott and W. A. Simril.—p. 78.
Use of Roentgen Ray in Diagnosis and Therapy of Faulty Ovulation. W. W. Williams.—p. 88.

Roentgenographic Diagnosis of Tumors of Glomus Jugularis.—Riemenschneider and associates present the histories of two patients with tumor of the glomus jugularis. Roentgenograms of the skull at first appear to reveal chronic sclerosing mastoiditis. Later there is massive destruction of the petrous pyramid, with or without a mass in the posterior nasopharynx. This destruction is most marked in the lower portion of the

pyramid with the ridge left as a shell above. Vertebral angiograms demonstrate the tremendous vascularity of the tumor and the displacement of normal structures as a result of the space-occupying lesion. The extreme vascularity of the tumor makes adequate biopsy difficult, but the typical clinical history and roentgenographic findings should make a tentative diagnosis possible. A recurring bloody polyp in the external canal and the roentgenographic picture of chronic sclerosed mastoiditis are presumptive diagnostic findings. If the tumor is localized to the middle and external ear, radical resection and cure should be possible in a fair proportion of cases. Destruction of the petrous pyramid or a soft tissue mass in the posterior nasopharynx probably indicates inoperability.

Am. Practitioner & Digest of Treatment, Philadelphia

4:1-88 (Jan.) 1953

Emergency Experiences in Epidemic of Food Poisoning. H. A. Solomon, S. I. Kreps, L. B. Burness and R. E. Winter.—p. 2.
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Effect of Surgery on Life Realization of Advanced Age Groups. B. F. Byrd Jr.—p. 25.
Headache Clinics IV: Use of Octin (Methylisooctenylamine) in Treatment of Headache. L. S. Blumenthal and M. Fuchs.—p. 31.
Practical Investigation of Diarrhea. I. B. Brick.—p. 35.
Treatment of Essential Hypertension with Hydrogenated Alkaloids of Ergot. R. F. Grenfell.—p. 39.
Heavily Nitrated Water, Methemoglobinemia and Adrenal Tumors as Found in Family with Multiple Endocrinopathies. A. W. Kilness. —p. 45.
Charcot Joint in Diabetes Mellitus. J. T. Paul.—p. 49.
Diagnosis of Pulmonary Disease: An Outline of Procedure. C. W. Tempel. —p. 52.

American Surgeon, Atlanta, Ga.

19:1-94 (Jan.) 1953

Problem of Carcinoma of Lung. M. E. De Bakey.—p. 1.
Some Interesting Tumors in Renal Region. G. J. Thompson.—p. 9.
Osteoid Osteoma of Lamina and Its Treatment. I. J. Jackson.—p. 17.
Treatment of Recurring Intestinal Obstruction by the Plication Procedure. E. J. Poth, S. R. Lewis and F. J. Wolma.—p. 24.
Technic of Adequate Common Duct Exploration Using New Type Flexible Probe and Dilator. J. H. Clark.—p. 33.
Annular Pancreas. K. B. Castleton, R. P. Morris and A. J. Kukral. —p. 38.
Partial Gastrectomy for Peptic Ulcer. H. C. Dodson Jr.—p. 47.
Diverticulitis or Carcinoma of the Colon? G. B. Starkloff and D. Bindbeutal.—p. 59.
*Clinical Significance of Prolapsed Gastric Mucosa. F. M. Spencer, G. F. Madding and L. R. Hershberger.—p. 67.
Femoral Arteriovenous Fistula with False Aneurysm: Report of Case with Early Restorative Operation. C. R. Lam.—p. 78.
Acute Pseudomembranous Enterocolitis Simulating Acute Surgical Diseases of the Abdomen. G. L. Hansbro and T. E. Ferrell.—p. 82.
Treatment of Hernias in Infants and Young Children. H. D. Cogswell and E. W. Czerny.—p. 87.

Clinical Significance of Prolapsed Gastric Mucosa.—Observations on a number of patients with prolapse of the gastric mucosa left Spencer and his associates somewhat confused about the significance of this condition, for it is not always clear whether the prolapse is responsible for the patient's symptoms. Experience in one case in particular impressed them with the fact that prolapsed gastric mucosa may occasionally explain upper abdominal pain and associated gastrointestinal symptoms. This case is reported, together with opinions collected in personal discussions and correspondence with internists and surgeons. The authors conclude that caution is indicated in evaluating prolapsed gastric mucosa. The clinician, on recognizing a prolapse of the mucosa, should look for a peptic ulcer, a prolapsing polyp, antral gastritis, or hiatal hernia. Prolapse of the gastric mucosa into the duodenum may be responsible for gastrointestinal symptoms, because it is capable of producing gastrointestinal bleeding or partial pyloric obstruction. When roentgenologic study reveals prolapse the finding should not be ignored, nor should great significance be attributed to it until other pathological conditions have been excluded. In patients who have an ulcer-like syndrome, ulcer treatment should be instituted. When the symptoms are not suggestive of peptic ulcer and ulceration cannot be demonstrated, the patient should be treated with a bland diet, avoiding factors known to stimulate gastric peristalsis, and antispasmodic preparations. Ganglionic blocking agents, such as methantheline bromide, are probably the most effective in the reduction of gastric motility, and should therefore provide maximum relief. Surgical treatment should be reserved for patients in whom prolapse is complicated by bleeding, pyloric obstructions, or severe pain that fails to respond to prolonged medical management.

Cancer Research, Chicago

13:1-100 (Jan.) 1953. **Partial Index**

Attempt to Induce Resistance in Inbred Strain of Mice by Ligation of Homologous Tumor. J. C. Fardon and J. E. Prince.—p. 9.
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Distribution of Stilbamidine in Livers of Normal and Sarcoma-Bearing Mice. E. L. Bennett, D. E. Pack, B. J. Krueckel and J. C. Weaver. —p. 30.
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Induction of Shope Papilloma in Transplants of Embryonic Rabbit Skin. H. S. N. Greene.—p. 58.
Insect Tumors Induced by Nerve Severance: Incidence and Mortality. B. Scharrer.—p. 73.
Inhibition of Liver Carcinogenesis with 3'-Methyl-4-dimethylaminoazobenzene in Hypophysectomized Rats. A. C. Griffin, A. P. Rinfret and V. F. Corsigilia.—p. 77.
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Circulation, New York

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Intramural Depolarization Potentials in Myocardial Infarction: Preliminary Report. M. Prinzmetal, S. R. Kennamer, C. McK. Shaw Jr. and others. —p. 1.
Nature of Cardiac and of Pulmonary Dyspnea. D. W. Richards Jr. —p. 15.
*Selection and Medical Management of Patients with Mitral Stenosis Treated by Mitral Commissurotomy. G. C. Griffith, H. Miller, R. S. Cosby and others.—p. 30.
Prevention of Plasma Cholesterol Elevation and Atheromatosis in Cholesterol-Fed Bird by Administration of Dihydrocholesterol. M. D. Siperstein, C. W. Nichols Jr. and I. L. Chaikoff.—p. 37.
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*Observations on Carotid Sinus Reflex and Angina Pectoris. A. S. Freedberg and J. E. F. Riseman.—p. 58.
Effect of Exercise on Coronary Blood Flow, Myocardial Oxygen Consumption and Cardiac Efficiency in Man. T. A. Lombardo, L. Rose, M. Taeschler and others.—p. 71.
Normal and Impaired Retinal Vascular Reactivity. H. O. Sieker and J. B. Hickam.—p. 79.
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Effect of Posture on Excretion of Water and Sodium by Patients with Congestive Heart Failure. T. A. Lombardo.—p. 91.
Urinary Output of Catechol Derivatives Including Adrenaline in Normal Individuals, in Essential Hypertension, and in Myocardial Infarction. F. R. Nuzum and F. Bischoff.—p. 96.
Right Auricular and Ventricular Pressure Patterns in Constrictive Pericarditis. P. N. G. Yu, F. W. Lovejoy Jr., H. A. Joos and others. —p. 102.
Parietal Focal Block: Experimental and Electrocardiographic Study. V. Alzamora-Castro, R. Abugattas, C. Rubio and others.—p. 108.

Selection and Management of Patients Treated by Mitral Commissurotomy.—A large group of patients with mitral stenosis can be treated medically, another group may be benefited by surgical treatment, and in still another surgical treatment may be harmful. Careful selection, preoperative preparation, team work by the cardiologist, anesthetist, and surgeon during the operation, and wise postoperative care will reduce the death

rate. All the manifestations of the rheumatic state should be considered in selecting patients for surgical treatment, and only those in whom the mitral orifice is narrowed and whose capacity for work has been diminished should be chosen. Aortic stenosis and mitral regurgitation of more than a minimal degree are definite contraindications to commissurotomy, as is evidence of marked muscle damage, because an impaired left ventricle may be unable to carry the increased load following the relief of the obstruction. Thromboembolism is a strong indication in favor of the procedure. The amputation of the left auricular appendage with the decrease in pooling in the left atrium is one of the great benefits resulting from mitral commissurotomy. Preoperative management consists in bringing the patient's nutrition and state of well-being up to their maximum levels. Operative treatment must not be undertaken while there is evidence of congestive failure, liver engorgement, or myocardial irritability other than auricular fibrillation. The cardiologist should watch the patient during anesthesia and throughout the operation; close cooperation will enable the surgeon to concentrate on his work while the anesthetist maintains the lightest possible anesthesia with full oxygenation and the cardiologist assumes complete responsibility for the function of the heart. Postoperatively, hydration must be maintained to prevent fever, tachycardia, and thromboembolism. The average hospital stay is 5 days preoperatively and 10 days postoperatively. Mitral commissurotomy was performed in 74 patients up to May 15, 1952. There were eight deaths among the first 35 patients and none in the other 39. Short-term clinical evaluation of the results in the surviving patients made by the cardiologist, the physiologist, and the surgeon indicates that about one-third were greatly improved; one-third were markedly improved; and one-third showed little or no evidence of change in the murmurs or in the physiological function of the heart, and have been slow in recovering from the operation. None was made worse, except for a mild reactivation of rheumatic fever in two patients.

Carotid Sinus Reflex and Angina Pectoris.—The effect of carotid sinus pressure on the duration and characteristics of induced anginal pain was studied in 13 patients. Some relief of cardiac pain was experienced by all 13 as a result of right or left carotid sinus stimulation. Relief began during or shortly after about six seconds of carotid sinus stimulation in 11 patients and terminated the anginal attack in those patients whose attacks usually lasted less than one minute. Four patients with attacks usually lasting from one to four minutes secured temporary (22 to 64 seconds) relief from carotid sinus stimulation, after which the anginal pain returned in complete intensity, without any significant change in the total duration of the attack. Pain disappeared from the right side of the chest during application of right carotid sinus pressure while persisting on the left side in one patient, and in another pain disappeared from the chest but persisted in the shoulder. These observations support the hypothesis that carotid sinus stimulation induces relief of cardiac pain by interruption of sympathetic reflex arcs or sensory pathways. No evidence was found to indicate that carotid sinus pressure relieves cardiac pain by inducing coronary artery vasodilation or by altering the discrepancy between myocardial demand and blood supply observed in an attack of angina pectoris. Continuous electrocardiographic studies carried out before, during, and after carotid sinus pressure failed to show any consistent relationship between a change in cardiac rate following carotid sinus pressure and the relief of cardiac pain. Marked cardiac slowing was obtained without relief of pain, and pain was sometimes relieved when cardiac slowing was absent or not significant. The diagnostic and therapeutic usefulness of carotid sinus pressure is reduced by the fact that it may have dangerous or even fatal consequences.

Georgia Medical Association Journal, Atlanta

42:1-64 (Jan.) 1953

Problems in Weight Bearing and Gait in Poliomyelitis. F. M. Bell.—p. 12.
Meckel's Diverticulum as Cause of Intussusception. B. B. Gay Jr., T. F. Leigh and J. V. Rogers Jr.—p. 15.
Non-Penetrating Injuries of Abdomen. T. W. Goodwin.—p. 19.
Treatment of the Alcoholic. J. N. Brawner Jr.—p. 21.

Journal of Applied Physiology, Washington, D. C.

5:247-310 (Dec.) 1952. **Partial Index**

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Effect of Exercise and Environment on Urine Secretion After Water Load. C. H. Wyndham, W. V. D. M. Bouwer, M. G. Devine and H. E. Paterson.—p. 285.

Journal of Aviation Medicine, St. Paul

23:545-636 (Dec.) 1952. **Partial Index**

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Electrocardiographic Studies on Human Subjects Breathing Oxygen at Extremely High Pressures. D. I. Mahoney and J. V. Kennedy.—p. 560.
Modifications of Excitability of Respiratory Centers in Course of Anoxemia: Consequences of Modifications in Treatment of Anoxemic Syncope. R. Grandpierre, C. Franck and R. Lemaire.—p. 566.
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Journal of Clinical Investigation, New York

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Metabolism of Glycine-2-C^{14} in Man: III. Urinary Excretion of C^{14} and Cumulative Radiation Dosimetry. N. I. Berlin, B. M. Tolbert and H. C. Lee.—p. 1.
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Distribution and Fate of Intravenously Administered Modified Human Globin and Its Effect on Blood Volume: Studies Utilizing I^{131} Tagged Globin. S. A. Berson, R. S. Yalow, J. Post and others.—p. 22.
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Relationship Between the Clearance and Plasma Concentration of Inulin in Normal Man. T. J. Kennedy Jr. and J. Kleh.—p. 90.
*Comparison of Coombs Test with Other Methods for Brucella Agglutinins in Human Serum. W. H. Hall and R. E. Manion.—p. 96.

Tests for Brucella Agglutinins in Human Serum.—Hall and Manion made comparative studies on serums from 104 adults to evaluate methods for demonstrating Brucella agglutinins. The methods included the tube dilution, rapid macroscopic slide (Huddelston), rapid slide (Castaneda), indirect Coombs' antiglobulin, "blocking," centrifugation and paper chromatographic method. They found that the tube dilution method is more sensitive than Huddelston's rapid macroscopic slide tests. Castaneda's rapid slide test is useful as a quick bedside method

to detect active human brucellosis, but it gives only a crude index of the quantity of agglutinin. The "blocking test" is seldom useful, because only very rarely does a patient with brucellosis have sufficient blocking antibody to obscure the results of the tube dilution agglutination test. The indirect Coombs' antiglobulin method is a sensitive but tedious and expensive procedure for titrating Brucella agglutinins. High speed centrifugation after incubation of serum-antigen mixtures yields a sensitivity equal to or greater than that of the Coombs' method, with greater speed and simplicity. Paper chromatography is a sensitive technique for detecting Brucella agglutinins in human serums, but its usefulness in differentiating "specific" from "nonspecific" agglutinins remains in doubt. The tube dilution method, with a standard Brucella antigen and standard immune serums as controls, is the most useful practical procedure for the demonstration of Brucella antigens.

Journal Lab. and Clinical Medicine, St. Louis

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Relation of Life Stress and Emotions to Human Sebum Secretion and to the Mechanism of Acne Vulgaris. T. H. Lorenz, D. T. Graham and S. Wolf.—p. 11.

Evaluation of Measurement of Cardiac Output and of So-Called Pulmonary Blood Volume by Dye-Dilution Method. J. T. Doyle, J. S. Wilson, C. Lepine and J. V. Warren.—p. 29.

Effect of Prolonged Administration of Radioactive Zinc on Pancreas. J. W. Sherrill and A. N. Wick.—p. 40.

Excretion of Water and Electrolytes in Patients with Essential Hypertension. W. A. Brodsky and H. N. Graubarth.—p. 43.

*Use of Cobaltous Chloride in Anemia Associated with Chronic Renal Disease. F. H. Gardner.—p. 56.

Maintenance Therapy of Pernicious Anemia with Vitamin B_{12}. G. C. Meacham and R. W. Heinle.—p. 65.

Combined Anticonvulsant Activity and Toxicity of Dilantin and N-Methyl-5-Phenylsuccinimide. G. Chen and C. R. Ensor.—p. 78.

Post-Transfusion Survival of Erythrocytes Stored in Solution of Ethylenediamine Tetraacetic Acid and Dextrose. C. C. Sprague, J. B. Shapleigh, S. Mayes and others.—p. 84.

Variation in Complement Fixation Antigen Production by Different Strains of Histoplasma Capsulatum Grown on Two Media. J. Schubert, L. Ajello, S. Stanford and V. Q. Grant.—p. 91.

Evaluation of Middlebrook-Dubos Hemagglutination Test. E. F. Rabe and W. S. Spicer Jr.—p. 98.

Migration and Oxidation-Reduction Activity of Leukocytes from Patients with Acute Disseminated Lupus Erythematosus. S. N. Chaudhuri and S. P. Martin.—p. 108.

Role of Cold Hemagglutinins in Frostbite. D. Weiner.—p. 114.

Duration of Penicillin Action in Relation to Its Concentration in Serum. H. Eagle, R. Fleischman and M. Levy.—p. 122.

Clinical Laboratory Studies in Experimentally-Induced Epidemic Nonbacterial Gastroenteritis. I. Gordon, J. K. Meneely Jr., G. D. Currie and A. Chicoine.—p. 133.

Prevention of Paralytic Poliomyelitis in Tonsillectomized Cynomolgus Monkeys by Human Gamma Globulin. J. M. Adams, R. A. Boak, C. M. Carpenter and others.—p. 142.

Recent Changes in Sensitivity of Micrococcus Pyogenes to Various Antibiotic Agents. G. M. Needham and D. R. Nichols.—p. 150.

Cobaltous Chloride in Anemia Associated with Azotemia.—The cause of the anemia associated with chronic azotemia is not known, but it is believed to be due to toxic inhibition of erythropoiesis and/or hemolysis. Since recent studies have suggested that cobalt is a nonspecific stimulant of erythropoiesis, this drug was given to patients with the anemia of azotemia to determine its therapeutic and toxic effects. It was felt that this type of therapy would be more satisfactory than the use of transfusions, since repeated transfusions frequently produce fever and anorexia, which increase the burden on the already poorly functioning kidney. It was also hoped to determine whether these patients felt subjectively improved with consistently higher hemoglobin levels. At first a 50 mg. uncoated tablet of cobaltous chloride was used. Because of gastrointestinal distress, however, a 20 mg. enteric-coated tablet was prepared, and patients were instructed to take the medication with meals. They were observed carefully for signs of gastrointestinal irritation that might result in vomiting and the added burden of extrarenal azotemia. The dosage was increased at weekly intervals to the patient's tolerance or to the level where a hematopoietic response was apparent. The daily doses ranged between 50 and 200 mg. Seventeen patients were studied for at least a four week period. In 18 additional patients the rapid decline in health with progression of azotemia and acidosis did not allow adequate evaluation or continuation of cobalt therapy. Most patients showed a significant erythropoietic response in one month and maximal values were reached in two to three months. The increased values declined to pretreatment levels when the drug was discontinued. No evidence was obtained to suggest that cobalt therapy had altered the course of the renal disease. Earlier reports had emphasized the nephrotoxic activity of cobalt in animals, but in those studies the amounts of cobalt given were far in excess of the oral dosages used in this group of patients. Effects on the kidney parenchyma from prolonged exposure to this metal in low concentration await further study.

Journal of Pediatrics, St. Louis

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Retention of Water and Electrolyte During Recovery in Patient with Diabetic Acidosis. D. C. Darrow and E. L. Pratt.—p. 688.

Deformity of Vertebral Bodies in Cretinism. P. R. Evans.—p. 706.

Osteogenesis Imperfecta Congenita: Connective Tissue Diathesis. R. H. Follis Jr.—p. 713.

*Vascular Complications of Juvenile Diabetes: Analysis of 40 Patients After 10 Years of Disease. H. G. Guild, W. Grubb, M. Y. F. Chu and J. B. Sidbury Jr.—p. 722.

Bronchial Obstruction and Bronchiectasis Complicating Primary Tuberculous Infection. J. B. Hardy, D. F. Proctor and J. A. Turner.—p. 740.

Further Studies of Effects of Citrate Feeding on Calcium, Phosphorus, and Citrate Metabolism of Rachitic Infants. H. E. Harrison and H. C. Harrison.—p. 756.

Congenital Obliteration of Bile Ducts: With Particular Reference to Dietotherapy. L. Krahulik, M. P. Shoob, S. Morales and others.—p. 774.

Carotenemia of Hypothyroidism. H. W. Josephs.—p. 784.

*Treatment of the Nonedematous Nephrotic Child with ACTH. B. Kramer, H. Goldman and L. Carson.—p. 792.

Physiology and Disorders of Carbohydrate Metabolism. V. A. Najjar.—p. 804.

Some Comments on Herpetic Infection in Children with Special Emphasis on Unusual Clinical Manifestations. T. F. M. Scott, L. Coriell, H. Blank and C. F. Burgoon.—p. 835.

*Hospital Cross-Infections and Their Control. M. H. D. Smith and C. G. Loosli.—p. 844.

Vascular Complications of Juvenile Diabetes.—The authors studied 40 diabetic children who had had their disease for 10 years or more with reference to vascular complications, chiefly retinal and renal. The purpose of the study was, first, to determine the incidence and the time of appearance of those complications and, second, to determine whether there was a correlation between the occurrence of complications and the extent to which the diabetes had been controlled. It was found that vascular complications of diabetes, especially those that can be detected in the retina, may be found relatively early in the course of juvenile diabetes. While the incidence of such complications increases with the passage of time, the time of appearance, severity of lesions, and rapidity of progression are modified by the degree of diabetic control. Patients with only fair or poor control may show lesions as early as 10 years after onset and rarely escape some evidence of vascular damage by the time the disease has been in progress for 15 years. Patients consistently well controlled may remain free of lesions for as long as 18 years and may show no more than minimal changes as long as 22 years after onset. Even in those who do not escape completely, the lesions are less rapidly progressive than in the groups not so well controlled. In children in whom the onset of diabetes occurs during the preschool period, good control is more easily established and maintained than in those in whom it occurs at a later date, when there has already been a taste of freedom from dietetic restrictions. Regularity of attendance at the clinic or the physician's office, which permits careful supervision and systematic training in the diabetic way of life, is an important factor in the maintenance of good control.

Corticotropin in Lipoid Nephrosis.—Treatment of lipoid nephrosis has been directed chiefly toward elimination of edema. Although other agents have induced diuresis, the results have been most consistent with corticotropin. The edema usually recurred, however, in a few weeks or months. Treatment with corticotropin also induced changes toward normality in the serum protein and lipid levels, the erythrocyte sedimentation rate, and albuminuria. With the return of edema, however, all these values returned to their previous levels. Kramer and associates decided to administer corticotropin to nonedematous nephrotic children, that is, to those in whom diuresis had been induced by administration of corticotropin over a period of

10 to 17 days. Diuresis either began while the drug was being administered or shortly after it was discontinued. After one or two weeks, a second course of corticotropin was begun, and the drug was given for another 10 to 17 days. The dosage used was 25 mg. every six hours except where previous experience indicated that a larger dose would be necessary or when the dose had to be reduced because hypertension developed. This pattern of two courses of treatment was chosen because it was felt that interruption of the corticotropin therapy might lessen the incidence of complications. The complications were, however, the same as those observed with single courses of corticotropin. Treatment of a nephrotic child in this manner seems to prolong the remission usually seen when corticotropin is given merely to obtain diuresis. More time will have to elapse before the persistence of improvement can be judged. There have been three deaths among the 20 patients treated.

Control of Cross Infections in Hospitals.—Smith and Loosli review the various efforts made to control cross infection in hospitals, but find that the ideas set forth in the recent memorandum of the Medical Research Council on the "Control of Cross-Infection in Hospitals" differ little from those expressed by Chapin 35 years earlier. The prevention of contact infection by "medical asepsis" is well-established. As to control of air-borne and dust-borne infections, the most carefully conducted studies have failed to produce convincing evidence that ultraviolet irradiation, oiling of floors and bed linen, and vaporization of glycols will reliably reduce the number of cross infections. Administration of chemotherapeutic and antibiotic drugs to patients for prevention of bacterial nosocomial infection may be effective temporarily but is likely to give rise to outbreaks of disease due to insusceptible micro-organisms. The one constructive concept formulated in recent years seems to be that of the "dangerous carrier": since patients with severely infected skin or nasal discharges seem the most dangerous to fellow patients and the staff, it seems logical to direct efforts toward isolating this type of patient. Unusually susceptible persons, such as premature infants and patients with extensive burns or weeping eczema, should be protected.

Journal of Urology, Baltimore

69:1-192 (Jan.) 1953. Partial Index

Renal Neoplasms: Enigma and Challenge. C. L. Deming.—p. 1.
Carcinoma in Polycystic Kidney. W. F. Johnson.—p. 10.
Spontaneous Bilateral Perirenal Hematoma. G. S. Link.—p. 13.
Cyto-Dynamic Properties of Urinary Neoplasms: III. Cultivation in Vitro of Carcinoma of the Kidney. R. G. Bunge.—p. 18.
*Abnormal Renal Mobility. A. F. Kaminsky, R. B. Roth and E. Hess.—p. 21.
Principle of Aortic Compression in Management of Massive Hemorrhage from Renal Pedicle After Nephrectomy. H. W. Scott Jr., J. R. Cantrell and P. L. Bunce.—p. 26.
Monilial Infection of Kidney: Case Reports. D. D. Albers.—p. 32.
Injury of Kidney in Children. H. O. Mertz.—p. 39.
Upper Urinary Tract Disease with Symptoms Simulating Herniated Nucleus Pulposus. M. Malament and R. C. Bunts.—p. 46.
Modern Treatment of Acute Renal Failure. S. A. Vest and R. A. Kelley.—p. 55.
Renal Insufficiency: Its Mechanism and Management. J. H. Harrison—p. 67.
Lumbar Ureterolithotomy. W. N. Taylor.—p. 77.
Hyperchloremic Acidosis of Ureterosigmoidostomies. A. D. Mitchell and W. L. Valk.—p. 82.
*Preliminary Report: Study of Effects of Banthine on Human Bladder. J. Lapides and A. Dodson Jr.—p. 96.
Vesical Neck Obstruction in Women. S. P. R. Hutchins.—p. 102.
Bladder Neck Obstruction in Young Male Adult. A. B. Peyton.—p. 109.
Leukoplakia of Urinary Bladder and its Association with Carcinoma. D. B. Connery.—p. 121.
Heat Factor as Cause of Hemoglobinemia in Transurethral Resections. C. Ferguson and C. D. Miller.—p. 128.

Abnormal Renal Mobility.—The normal kidney has an average range of motion up to 5 cm.; mobility exceeding this arbitrary limit is considered to be unusual. Reviewing 241 cases of abnormal renal mobility seen over a period of five years, Kaminsky and associates concluded that uncomplicated renal ptosis is rarely an indication for surgery. The movable kidney may be an abdominal mass that disturbs the patient, but under ordinary circumstances reassurance is more to the point than nephropexy. When nephroptosis, by virtue of angulation and obstruction of the ureter or ureteropelvic junction, is an underlying cause or a contributing factor in the production of urinary stasis, the kidney must be suspended. The one feature of nephroptosis that to a large degree defies satisfactory analysis is the factor of pull or drag on the renal pedicle. A reasonably rigid selection in the series of 241 cases led to surgical treatment in 33 instances. In 30 of these cases the surgical treatment consisted of nephropexy with partial renal denervation. Follow-up survey in these 30 cases has shown that most of the patients have obtained relief from symptoms.

Effects of Methantheline on Human Bladder.—Workers investigating the effect of methantheline (banthine®) in treatment of peptic ulcer observed acute urinary retention in several males with benign prostatic hypertrophy who received the drug orally. In view of the action of methantheline in blocking impulses transmitted through the parasympathetic nerves, its relatively low toxicity and its effectiveness when administered orally, it was decided to investigate its effect on normal and abnormally functioning urinary bladders to determine its usefulness in treatment of neurogenic bladder disorders. The drug was administered both orally and intravenously to human subjects. A cystometric determination was obtained prior to drug administration and within 10 minutes after intravenous injection or within three to five days after the initiation of oral therapy. The intravenous doses varied from 100 to 150 mg., while the oral dose varied from 25 to 100 mg. given four times a day. In some of the patients who received methantheline orally, administration of the drug was stopped, and after five days another cystometric examination was made. Observations were made on normal bladders, uninhibited neurogenic bladders, and reflex neurogenic bladders. It was found that methantheline can block all the motor impulses to the bladder, resulting in complete urinary retention. In moderate doses methantheline is most effective therapeutically in the uninhibited neurogenic bladder, a condition frequently encountered in patients with multiple sclerosis, hemiparesis due to cerebrovascular accidents, luetic paresis (not tabes), postoperative cordotomy, and congenital neurogenic enuresis. Methantheline, in these patients, causes a disappearance of uninhibited contractions and results clinically in a decrease in frequency of urination, with complete disappearance of urgency and incontinence without producing urinary retention. Large doses of methantheline in conjunction with distention of the bladder are efficacious in increasing the bladder capacity of paraplegics with spastic reflex neurogenic bladders.

Kentucky State Medical Assn. Journal Bowling Green

51:1-44 (Jan.) 1953

Geriatric Surgery: Some Observations of Surgical Patients in Older Age Groups. G. L. Simpson.—p. 1.
*Considerations of Surgical Treatment of Carcinoma of Cervix Uteri. L. A. Gray.—p. 5.
When a Psychiatric Case Walks Into Your Office. W. K. Keller.—p. 9.
Histoplasmosis. J. W. Armstrong.—p. 12.
Seasonal Incidence of Acute Myocardial Infarction in Kentuckiana Area. M. M. Weiss.—p. 14.
Doctor's Day in Court. L. R. Curtis.—p. 16.
Complications of Biliary Tract Surgery. J. D. Hancock.—p. 21.

Surgical Treatment of Carcinoma of Cervix Uteri.—The Wertheim radical panhysterectomy with excision of the pelvic lymph nodes was performed in 17 women between the ages of 29 and 54 with carcinoma of the cervix uteri. The preoperative clinical impression was that 15 patients had stage 1 carcinoma and the remaining 2 had stage 2 carcinoma. After the postoperative study of the removed lymph nodes, stage 1 carcinoma was demonstrated in nine, stage 2 carcinoma in one, and stage 3 carcinoma, with metastases in the lymph nodes near the pelvic wall, in seven. Twelve of these patients had preoperative x-ray treatment with an approximate tumor dose of 3,000 r to the region of the lymph nodes, and 2 of them were also treated with radium preoperatively. Five of these 12 patients apparently had viable metastases in the lymph nodes. This large percentage of relatively insensitive metastases in lymph nodes suggests that radical surgery with lymph node dissection should be considered in cases in which surgery is feasible. Preoperative x-ray therapy to the parametrium appears logical to destroy any tumor in the connecting lym-

phatics, as these must be broken across in the dissection. The tumor in the lymphatics is usually radiosensitive. It is emphasized that ordinary total hysterectomy has no place in treatment of carcinoma of the cervix. The radical surgery is time-consuming and requires expert administration of the anesthesia and available blood for multiple transfusions. The results from carefully planned irradiation therapy with properly distributed local radium and multiple ports for x-ray treatment aimed at the obturator, hypogastric and external iliac lymph node areas are not to be deprecated, particularly in cases of carcinoma in an advanced stage and in elderly obese patients or in the presence of medical contraindications to surgical treatment. With great care and continued observation of the patients, extremely gratifying results follow in more than half of the cases. Radiation-insensitive tumors, local recurrences after therapy, and the problem of metastases in lymph nodes make the author suspect that a carefully planned combined attack should be used in early favorable cases. The greatest possibility of increasing the cure rate lies in early diagnosis. This can only be done by the routine use of the biopsy forceps on every erosion of the cervix before cauterization. The only exception is the soft virginal erosion in very young women. When the lesions are detected at the earliest possible stage, it is possibly immaterial whether irradiation or surgery is used.

Nebraska State Medical Journal, Lincoln

38:1-32 (Jan.) 1953

Certain Radiological Aspects of Abdominal Pain in Children. C. Z. Berman.—p. 3.

Differentiation Between Causes of Atrophy of Intrinsic Muscles of Hand. A. I. Finlayson.—p. 10.

Stenosis of Esophagus Due to Ingestion of Corrosives. D. Brigham and H. M. Jahr.—p. 14.

Problems Relating to Recognition of Hydronephrosis in Everyday Medical Practice. R. M. Nesbit.—p. 17.

Reconstruction After Traumatic Deformity of the Ear. W. P. Kleitsch. —p. 21.

New England Journal of Medicine, Boston

248:81-124 (Jan. 15) 1953

Pulmonary Function After Segmental Pulmonary Resection for Bronchiectasis. B. E. Etsten, R. H. Overholt, J. H. Walker and R. N. Reynolds.—p. 81.

Total Adrenalectomy for Reactivated Carcinoma of Prostate. J. H. Harrison, G. W. Thorn and D. Jenkins.—p. 86.

*Acute Infectious Lymphocytosis: Report of Two Cases in Same Family. H. D. Riley Jr.—p. 92.

Drug Fever Due to Quinidine. O. A. Rose, A. Vogl and A. I. Turtz. —p. 96.

Use of Digitalis in Infants and Children: Clinical Study of Patients in Congestive Heart Failure. A. S. Nadas, A. M. Rudolph and J. D. L. Reinhold.—p. 98.

Twin Pregnancy Resulting in Birth of Viable Infant and Blighted Fetus. T. N. Zervas.—p. 105.

Apparatus for Continuous Blood-Pressure Observation. R. W. Alman and J. F. Fazekas.—p. 105.

Acute Infectious Lymphocytosis. — Infectious lymphocytosis was originally thought to be a variant of infectious mononucleosis. Its chief characteristic is a relative increase in the number of the small mature lymphocytes. Two cases are reported in brothers, aged 4 and 3. Both patients showed signs of upper respiratory infections, and the course was not affected by penicillin in one case or by aureomycin in the other. The maximum white blood cell counts were 32,800 and 29,750. The clinical picture of infectious lymphocytosis may be similar to that of infectious mononucleosis, although patients with the latter disorder generally show severe throat involvement, fever, marked malaise, generalized lymphadenopathy, splenomegaly, and occasionally rash and jaundice. The main distinguishing features are the presence of large, abnormal lymphocytes or mononuclear cells and a positive heterophil-antibody agglutination (Paul Bunnel test) in infectious mononucleosis; in infectious lymphocytosis, on the other hand, the lymphocytes are usually small and mature, and the Paul Bunnel test is negative. Infectious lymphocytosis may also suggest pertussis, but failure to grow Hemophilus pertussis on Bordet-Gengou medium will rule out whooping cough. Lymphatic leukemia, especially the acute type, can be differentiated from infectious lymphocytosis by the clinical picture of fever, lymphadenopathy, splenomegaly, hemorrhagic tendencies, and progressive downhill course, as well as by the presence of circulating lymphoblasts and the diminution in erythrocytes, hemoglobin, and platelets. The hematological changes of infectious lymphocytosis usually persist much longer than the symptoms; most patients have an abnormally high leukocyte count for two to five weeks, but lymphocytosis has been noted as long as seven months. In both the cases reported here the white cell count remained elevated for 19 to 26 days. The prognosis is excellent, and complete recovery without sequelae is the rule.

North Carolina Medical Journal, Winston-Salem

14:1-48 (Jan.) 1953

Indications for Sterilization of Women. J. F. Donnelly and F. R. Lock. —p. 1.

Management of Cystic Disease of Lung. W. C. Sealy.—p. 6.

Management of Symptomless Intrathoracic Lesions. P. W. Sanger.—p. 9.

Sins of Commission in Pediatric Practice. R. B. Lawson and J. B. Reinhart.—p. 14.

Some Concepts of Acne Vulgaris and Its Therapy. M. E. McRae.—p. 17.

Use of Intravenous Procaine Hydrochloride in Medical and Surgical Conditions. A. G. Crumpler.—p. 21.

Psychiatric and Psychologic Evaluation of 64 Youthful Offenders. W. P. Wilson and L. B. Hohman.—p. 26.

Treatment of Traumatic Paraplegia. E. Alexander Jr.—p. 32.

Oral Surgery, Oral Medicine & Oral Path., St. Louis

6:1-242 (Jan.) 1953. Partial Index

*Value of Roentgenograms in Diagnosis of Tumors of the Jaws. E. C. Stafne.—p 82.

Diagnosis and Radiotherapy of Cancer of the Mouth. M. Cutler.—p. 93.

Newburgh-Kingston Caries Fluorine Study: IV. Dental Findings After Six Years of Water Fluoridation. D. B. Ast and H. C. Chase.—p. 114.

Investigative Tools in Study of Calcium Metabolism in Man: Balance Studies, Calcium Tolerance Test, Radioactive Calcium, and Complexing Agents. A. Schilling and D. Laszlo.—p. 139.

Dental Stigmata of Prenatal Syphilis. R. V. Bradlaw.—p. 147.

Giant-Cell Reparative Granuloma, Traumatic Bone Cyst, and Fibrous (Fibro-Osseous) Dysplasia of the Jawbones. H. L. Jaffe.—p. 159.

Leontiasis Ossea. L. R. Cahn.—p. 201.

Questionable Adamantinocarcinoma of the Mandible. S. J. Behrman. —p. 223.

Lymphosarcoma of Maxilla. H. I. Calman.—p. 232.

Malignant Melanoma Metastatic to the Mandible: Report of Case. L. I. Bluestone.—p. 237.

Roentgenograms in Diagnosis of Tumors of Jaws.—When routine dental roentgenologic examination reveals a jaw lesion, lateral jaw, occlusal, and other supplemental roentgenograms should be made. Dental roentgenographic examination with the standard intraoral dental film reveals minimal alterations in the trabecular pattern that are not discernible in the extraoral roentgenograms. Such changes may be evidence of a generalized skeletal disease. The author mentions the case of a man in whom roentgenologic examination of the teeth revealed an abnormal trabecular pattern characteristic of hyperparathyroidism. These lesions heal following treatment of hyperparathyroidism, whereas surgical eradication, in the belief that they represent a local lesion, has been followed by recurrences. When the roentgenogram reveals multiple lesions of the jaws, the presence of some form of polycystic disease should be suspected, and the patient should be advised to undergo further examination for the purpose of ruling out endocrine dysfunction, granulomatous disease, multiple myeloma, and other conditions in which multiple skeletal lesions may occur. The roentgenographic appearance of a lesion varies with the skeletal structure in which it occurs. Because of the anatomic difference between the maxilla and the mandible, similar pathologic lesions may present dissimilar roentgenographic appearances in these two structures. To add to the confusion, like lesions occurring within the same structure may present a varied picture, for example, ameloblastoma of the mandible. After discussing ameloblastoma of the mandible in greater detail, the author mentions lesions that resemble multilocular ameloblastoma, such as giant cell tumor, fibromyxoma, myeloma, and central angioma. The central feature of the resemblance is that they are multilocular. The roentgenographic

appearance of an idiopathic cystic cavity of the mandible may stimulate that of a solitary tumor of the jaws. The origin and nature of the idiopathic cystic cavity is still obscure, but the author suggests that it may be a developmental defect. The author also comments on translucent marrow spaces. The cooperation of clinician, roentgenologist, and pathologist is required for the diagnosis of tumors of the jaws.

Postgraduate Medicine, Minneapolis

13:89-184 (Feb.) 1953

"Cardiac Asthma." J. C. Meakins.—p. 89.
Changing Pattern of Pulmonary Disease. H. L. Israel.—p. 92.
Valvular Heart Disease in Older People. M. W. Anderson.—p. 101.
Detachment of Retina: Schneider Eye Foundation Presentation. J. H. Dunnington.—p. 107.
Problems in Thoracic Surgery. J. W. Gale.—p. 111.
Bleeding During Pregnancy. W. A. Scott.—p. 117.
Surgical Removal of Foreign Bodies with Aid of Stereoscopic Fluoroscopy: Report of Case Involving Needle in Pericardial Cavity. C. Santos.—p. 123.

Rocky Mountain Medical Journal, Denver

50:1-82 (Jan.) 1953

Early Practice of Medicine and Surgery in Ogden. E. Rich.—p. 23.
Differential Diagnosis in Rheumatic Diseases. C. J. Smyth.—p. 31.
The Chronically Ill. V. Kassel.—p. 37.
New Risks Bring New Insurance Forms: Part 1. L. A. Beck.—p. 40.

South Carolina Medical Assn. Journal, Florence

49:1-32 (Jan.) 1953

Inhalation Anesthesia. J. M. Brown.—p. 1.
Role of the EKG in General Practice. J. C. Shecut.—p. 4.
Psychiatric Component in Organic Disease. O. R. Yost.—p. 8.
The Key to Peace. C. Manion.—p. 12.

Southern Medical Journal, Birmingham, Ala.

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*Pulmonary Insufficiency in the Newborn. H. Morton, G. R. Hennigar and L. E. Sutton Jr.—p. 1.
Recent Developments and Future Trends in Field of Orthopedic Appliances. R. H. Alldredge.—p. 7.
Bronchogenic Carcinoma. J. D. Trader and E. T. Odom.—p. 12.
Better Tonsillectomies and Adenoidectomies: Fewer Postoperative Hemorrhages. E. H. Jones.—p. 15.
Milker's Nodules. E. P. Cawley, C. W. Whitmore and C. E. Wheeler.—p. 21.
Prophylaxis of Peptic Ulcer. M. O. Rouse.—p. 23.
Adequate Operation for Carcinoma of the Stomach. F. E. Walton.—p. 28.
Diagnosis and Treatment of the Infertile Couple. F. A. Simmons.—p. 33.
Uterine Curettage, Its Development and Use. C. J. Lund.—p. 39.
Medicine in the Small Town. P. Williamson.—p. 42.
The Medical Profession and the Public. L. H. Bauer.—p. 47.
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Suggestions in Coordinating the Study of the Psyche and the Soma. R. E. Semmes.—p. 51.
Emotional Aspects of Medical Rehabilitation. A. R. Dawson.—p. 53.
Rehabilitation of the Amputee Patient. D. A. Covalt.—p. 57.
Human Relations in Industry. R. L. Wells.—p. 60.
Ocular Lesions in Children Simulating Retinoblastoma: Report of 14 Cases of Pseudoglioma. J. J. Stokes.—p. 63.
Surgical Treatment of Hemifacial Spasm. G. O. Proud.—p. 66.

Pulmonary Insufficiency in the Newborn.—Autopsy reports indicate that over 50% of neonatal deaths in both full-term and premature infants result from pulmonary disturbances. The chief causes of pulmonary insufficiency in infants are primary or fetal atelectasis, secondary or resorption atelectasis, pulmonary hyaline membranes, vernix pneumonia with membrane formation, alveolar dysplasia, and mononuclear pneumonia. The authors review the cases of 200 infants, both premature and full-term, that died of various pulmonary complications during the first month of life. These were obtained from a series of 1,700 consecutive autopsies. Not less than four lung sections were studied in each case. The authors found that in this series the chief cause of death in the immature prematurely born infant is primary atelectasis; in the larger prematures it is hyaline membrane disease with atelectasis; while in the full-term infants it is vernix pneumonia. Immediate use of the broad spectrum antibiotics may be lifesaving in vernix pneumonia. The authors feel that alveolar dysplasia as a histological entity remains a highly controversial subject. They observed two cases strongly suggestive of persistent pulmonary mesenchyme and with what appeared to be greatly thickened alveolar septums. Clinically, the following characteristic picture prevails: the near term or term infant is cyanotic, with difficult respiratory exchange from birth, yet lives from one to two weeks with no evidence of congenital heart disease and with no clearing of the cyanosis and then suddenly dies. The authors suggest further investigations on the concept of alveolar dysplasia. Mononuclear pneumonia, or interstitial pneumonitis, usually occurs in infants about 1 year old, and it is becoming well documented as a cause of sudden death or of a rapidly fatal illness in infancy. These infants are well nourished and well developed, giving a history only of mild to moderate coryza of from one to seven days' duration, following which the infant may be found dead in the crib or in a shock-like state with irregular respirations. In the latter case death occurs either on the way to the hospital or on arrival. At autopsy the lungs show scattered red-purple areas of consolidation.

U. S. Armed Forces Med. J., Washington, D. C.

4:1-156 (Jan.) 1953. Partial Index

Isoniazid Therapy in Pulmonary Tuberculosis: Preliminary Report. F. W. Pitts, F. L. Miller, W. E. Dye and others.—p. 1.
Dynamic Cytology in Experimental Medicine. C. M. Pomerat.—p. 11.
Intravascular Thrombosis of Electric Origin. P. N. Sawyer and J. W. Pate.—p. 23.
Problem of Burns in Disaster. C. Artz, E. Reiss, J. H. Davis and W. H. Amspacher.—p. 39.
Iatrogenic Disease in Soldiers. H. A. Segal.—p. 49.
Predicting Efficiency of Problem Soldiers. J. W. Burkett.—p. 67.
*Ocular Fatigue in Radar Operator. R. S. Riffenburgh.—p. 71.
Effective Temperature as Measure of Heat Effect. G. A. Heffernon, H. J. Hittner and S. L. Kocis.—p. 73.
Hydrocortisone in Rheumatoid Arthritis. W. C. Berry and J. F. Benson.—p. 99.
Torsion of Spermatic Cord Among Men of Military Age. C. L. Deming and B. G. Clarke.—p. 105.
Clinical Evaluation of Phenylbutazone. R. M. Patterson, J. F. Benson and P. L. Schoenberg.—p. 109.
Electromyogram in Confirmatory Diagnosis of Pseudoparalysis. J. Goodgold.—p. 113.
Hepatic Amebiasis: Abscess and Probable Rupture Into Peritoneum with Survival. H. A. Braun and R. B. Stonehill.—p. 119.
Paget-Schroetter's Syndrome. R. C. Ziss.—p. 127.
Penetrating Wounds of the Heart. J. J. Wells.—p. 131.
Traumatic Asphyxia. L. M. Nyhus and O. S. Cook.—p. 137.
Hemangioma of Glans Penis. J. W. Lane.—p. 139.
Posttraumatic Mediastinal Hematoma. J. M. Hanner and F. E. Glauser.—p. 141.
Rupture of Spleen in Patient with Malaria. F. Perez-Pina, J. B. Hartney and S. L. Zimmerman.—p. 149.

Ocular Fatigue in the Radar Operator.—A large percentage of radar operators presented themselves at the eye clinic with complaints of tiring and headache during or following their work. The author feels that no man should have to watch the radar gear for more than one-half hour at one sitting, and a shorter time than this is probably to be preferred. This does not mean more men on watch, but more frequent change-offs. If a unit is shorthanded, it is not necessary for the man to have complete rest, only ocular rest. Since posture is a factor in tiring, the seating should be such that the operator can be relatively relaxed. At certain speeds of sweep of the radar, tiring is more rapid, but further study is necessary to determine the optimum speed, combining maximum comfort and efficiency in picking up contacts. The operator usually watches the screen in the most nearly complete darkness obtainable, but apparently complete darkness is not advisable. The optimum level of contrast between the screen and the surroundings is another factor that needs further investigation. It might be advisable to have available near the radar apparatus red goggles, similar to those used by pilots for dark adaptation prior to night flying. When it is necessary to leave the relatively darkened radar area, these would lessen the discomfort of sudden exposure to bright sunlight. They would also make the adaptation to a functioning level quicker on return to reduced illumination.

FOREIGN

Acta Medica Scandinavica, Stockholm

144:165-246 (No. 3) 1952. **Partial Index**

*Roentgen Irradiation of the Pituitary in Cushing's Syndrome: with Brief Discussion of Pathogenesis of the Syndrome. S. G. Johnsen.—p. 165.
Coronary Thrombosis and Other Forms of Circulatory Insufficiency Coinciding with Cerebral Apoplexy. H. Stürup.—p. 189.
Renal Excretion of Ketone Bodies II. A. Warming-Larsen.—p. 197.
Hematologic Changes Associated with Immune Response in Man. S. Pariser, R. A. Zucker and L. M. Meyer.—p. 201.

Roentgen Irradiation of Pituitary in Cushing's Syndrome.—Roentgen irradiation to the pituitary was given to one 44-year-old man and 10 female patients between the ages of 15 and 60 with almost all of the symptoms of fully developed Cushing's syndrome and one 11-year-old girl with mild Cushing's syndrome complicated by enormous obesity. The total x-ray dose administered varied from 6,000 r to 15,900 r, and six of the patients received a total dose of 9,000 r. Three patients who were followed for 7 to 12 years recovered completely. Three other patients probably recovered. Four patients were improved temporarily, and two were therapeutic failures. Larger irradiation doses than those previously recommended have been used by the author and presumably explain why the results are better than those reported by other workers. The complete recovery observed in some of the author's patients after intensive roentgen irradiation suggests that at least in certain cases there must be a pathological process in the pituitary that is roentgen sensitive and that manifests itself not only by excessive stimulation of the adrenal cortex but also by suppression of the normal hormone production (gonadotrophin) of the basophilic cells. The response of the adrenal cortex to the excessive stimulation by the pituitary may be reversible and cortical hyperfunction may cease as a consequence of roentgen irradiation, with resulting recovery of the patient. In other cases, the excessive pituitary stimulation might induce irreversible changes, i. e., the cortical cells would then develop an autonomic production, independently of the pituitary, and consequently treatment directed against the latter would be ineffective. As a result of this concept and the experience in his cases, the author recommends that intensive roentgen irradiation of the pituitary should be the primary treatment in Cushing's syndrome, partly because recovery is obtainable in some cases and partly because the irradiation of the pituitary may presumably be of importance for the reliability of the results obtained with secondary adrenalectomy.

Annals of Rheumatic Diseases, London

11:257-364 (Dec.) 1952

Effects of ACTH and Cortisone on Anaemia of Rheumatoid Arthritis. J. O. P. Edgcumbe and O. A. N. Husain.—p. 257.
Rheumatoid Arthritis in Male Patients. J. Forestier and F. Jacqueline.—p. 264.
Clinical Investigation of the Value of Synthetic Hyaluronidase Inhibitors in Rheumatoid Arthritis. L. Hahn, S. Thune and E. Truedsson.—p. 272.
Value of Intra-Articular Injections in Osteo-Arthritis: Controlled Series. M. H. L. Desmarais.—p. 277.
Collagenous Pseudotumours of the Hands. O. C. Kestler.—p. 282.
Osteophytosis of Lumbar Spine: Comparison Between Incidence in Saskatchewan, Canada, and Bristol, England. O. D. Beresford.—p. 289.
Blood Glutathione Levels in Rheumatoid Arthritis. D. Watson, D. S. Bidmead and G. D. Kersley.—p. 292.

Belgisch Tijdschrift voor Geneeskunde, Leuven

8:1057-1104 (Dec. 1) 1952

Dysgerminoma. J. Figoureux.—p. 1057.
*Chronic Thyrotoxic Myopathy. K. Vuylsteek and J. Bekaert.—p. 1065.
Atomic Bomb Explosions and Their Results in the Medical Field. J. De Backer.—p. 1069.

Chronic Thyrotoxic Myopathy.—The fact that two cases of muscular atrophy in patients with hyperthyroidism were observed by Vuylsteek and Bekaert within two months seems to suggest that the concurrence of these two disorders is not rare. The authors believe that the majority of patients with severe exophthalmic goiter have a certain degree of myasthenia that is usually not very evident because the atrophy involves uniformly all skeletal muscles. In the condition referred to as chronic thyrotoxic myopathy, the muscular atrophy is more circumscribed, being usually restricted to the musculature of the pelvic and shoulder girdles. The muscle cells undergo atrophy, fatty infiltration, vacuolization, and nuclear degeneration, and they lose their transverse striations. The authors point out that chronic thyrotoxic myopathy has been discussed by a number of American observers, who emphasized among other factors that in patients with this form of myopathy the symptoms of thyrotoxicosis are frequently mild but the myopathy dramatically improves following adequate treatment of the thyrotoxicosis. For this reason a primary disorder of the thyroid should be considered whenever there is muscular atrophy.

Brain, London

75:433-606 (Dec.) 1952

Significance of Perceptual Rivalry Resulting from Parietal Lesion. D. Denny-Brown, J. S. Meyer and S. Horenstein.—p. 433.
Some Aspects of Human Orientation in Space: Sensation and Movement. W. Gooddy and M. Reinhold.—p. 472.
Cortical Representation of Motor Units. E. G. T. Liddell and C. G. Phillips.—p. 510.
Kernicterus. J. Gerrard.—p. 526.
Residual Neurons in Human Thalamus Following Hemidecortication. T. P. S. Powell.—p. 571.
Disturbances of Sensation Occurring in Area not Innervated by Severed Nerve. S. Sunderland.—p. 585.
Unusual Disturbance of Muscle Function Resulting from Severance of Peripheral Nerves. S. Sunderland.—p. 589.
Muscular Fasciculation and Reactive Myotonia in Polyneuritis. C. Worster-Drought and F. Sargent.—p. 595.

British Medical Journal, London

1:1-54 (Jan. 3) 1953

Infection in Newborn Baby. A. Moncrieff.—p. 1.
*An Epidemic of Influenza Due to Virus B. T. Anderson, N. R. Grist, J. B. Landsman and others.—p. 7.
Staphylococcal Pyothorax in Infants. F. Rackow.—p. 11.
Immunity of Newborn: Study of Transfer of Anti-Streptolysin from Mother to Foetus During Pregnancy. J. Murray and R. M. Calman.—p. 13.
*Natural History of Cystic Disease of Breast Treated Conservatively. D. H. Patey and A. W. Nurick.—p. 15.
A.C.T.H. in Diagnosis of Adrenal Insufficiency (Thorn Test). R. R. de Mowbray and P. M. F. Bishop.—p. 17.
Toxic Reactions Due to Intravenous Iron. I. M. Librach.—p. 21.
Auricular Paroxysmal Tachycardia in Childhood. T. Wright.—p. 25.
Effect of Hydralazine in Hypertension. M. A. Khan.—p. 27.
Effect of P.A.S. on Thyroid Gland. R. R. Hamilton.—p. 29.

Epidemic of Influenza Due to Virus B.—Serological studies and other epidemiological investigations show that virus B infection was prevalent in Glasgow during late February and March, 1952. The course of the epidemic may be judged from morbidity and mortality statistics for the period from Dec. 1, 1951, to March 31, 1952. The figures for new claims to the Ministry of National Insurance show that in the early weeks of 1952 there was a gradual increase in sickness that became more accentuated between the 8th and 12th weeks of the epidemic and ended in the 13th week. Reports of pneumonia began to increase steadily in the 1st week of the period, started to rise more rapidly in the 7th week, reached a peak in the 9th, and declined in the 13th. The number of deaths from respiratory disease, excluding tuberculosis, which began to rise in the 4th week, showed a moderate increase in the 9th, 10th, and 11th weeks. Antibodies to virus B were present in a high proportion of the patients admitted to the pneumonia wards. Indications were that there was either a high virulence of virus B or an increased susceptibility of the population. Comparison of the figures for this epidemic with those for the 1950-1951 virus A epidemic showed that similar numbers of persons were affected in both and that the number of pneumonia cases reported was almost the same. The age distribution of patients who died of pneumonia, however, differed: in the virus A epidemic, which had a much higher mortality rate, most cases occurred in the youngest and oldest groups. Three interesting facts were disclosed by a study of the meterological conditions: (1) the relative humidity fell from a rather high reading to a very low figure during the week in which the epidemic is assumed to have begun; (2) the minimum temperature was unusually low in the period immediately preceding; and (3) the average daily range of temperature was

much greater than usual for the season. Climatic changes of this kind may induce variations in resistance favoring invasion by a virus of normally low virulence, such as influenza virus B. Study of school attendance records indicates that the infection spread through the city from a focal area on the Clyde. This area contains a number of industries and a dock into which the bulk of the coastal and continental trade is received, and its population is overcrowded and badly housed. The World Health Organization reported that virus B influenza was prevalent on the continent from mid-November of 1951 on, and the virus may have been introduced into the city from an overseas ship, although small groups of cases occurred in parts of England during the same period.

Cystic Disease of Breast Treated Conservatively.—Study of 76 patients with cystic disease of the breast during a 20 year period supports the belief that the condition is essentially benign and can be safely treated by simple aspiration if certain precautions are observed. The diagnosis was established in 69 of these cases by aspiration and in the remaining 7 by operation (local excision), which was performed because either aspiration had failed or the lesion was mistaken for a solid lump. Follow-up of 65 of the patients showed that carcinoma of the breast did not develop in 64; in one it developed in the opposite breast. The infrequency with which cystic disease and carcinoma of the breast are associated is further indicated by analysis of 810 cases of carcinoma of the breast seen during 1930-1950; only 10 patients had a previous history of cyst. Cysts showing evidence of intracystic tumor, however, should be regarded as possibly malignant and should be operatively explored. The presence of tumor in a cyst may be shown in various ways, as for instance, by a blood-stained discharge from the nipple; sometimes, it will be discovered only after the associated tumor has been diagnosed and surgically removed. Intracystic tumor should be suspected on aspiration if blood is found in the aspirated fluid, if a residual lump persists after aspiration, or if a cyst refills within a few weeks of aspiration. Intracystic tumors were found in eight of the total of 886 patients, but in none of them did the tumor develop in a cyst previously treated by aspiration; on the contrary, in most cases, the tumor probably preceded and even caused the cyst. Cysts may or may not recur, but the tendency toward cyst development often disappears, sometimes after only one manifest cyst and sometimes after a succession of cysts. Aspiration, therefore, which is a conservative, nonmutilating procedure imposing only a minor and often temporary burden on the patient, is the treatment of choice for cystic disease of the breast.

1:55-116 (Jan. 10) 1953

Epidemiology of Some Skin Infections. R. Cruickshank.—p. 55.
*Triethylene Melamine in Human Malignant Disease: Results with Oral Administration of Enteric-Coated Tablets. E. Paterson, P. B. Kunkler and A. L. Walpole.—p. 59.
Tuberculosis Case-Finding by Tuberculin-Testing of Infant-School Children. I. A. MacDougall, J. R. Mikhail and W. H. Tattersall.—p. 64.
Acute Chest in General Practice. J. Fry.—p. 68.
Dissecting Aortic Aneurysm: Varied Clinical Picture. R. K. MacCuish.—p. 71.
Leaking Abdominal Aneurysms: Two Unusual Cases. J. W. Betts and B. C. Rowlands.—p. 73.
Food Supply, Body Weight, and Activity in Great Britain, 1943-9. J. M. Harries and D. F. Hollingsworth.—p. 75.
Haemolytic Anaemia Treated by A.C.T.H., Cortisone, and Splenectomy. J. D. Aitchison.—p. 78.
Diffuse Phlebosclerosis with Calcification. A. Charan.—p. 80.

Triethylene Melamine Orally in Human Malignant Disease.—Triethylene melamine has been used both intravenously and orally for the palliation of chronic malignant disease. The authors describe animal experiments with this drug and therapeutic studies on 43 patients, pointing out that the clinical trial of a new substance presents difficulties. One is the very advanced stage of the disease in patients selected for treatment, and another is the dose level. The trial of enteric-coated tablets revealed a reasonable consistency between dose and effect when doses were determined on a weight basis. A beneficial effect was obtained in Hodgkin's disease, in chronic leukemia, and in two other cases of reticuloendothelial disease; no good effect has been obtained in the tumors of epithelial or connective tissue origin. In Hodgkin's disease between 0.2 and 0.3 mg. per kilogram of body weight was given either undivided or spread over two or three days. Treatment should not be given in the presence of leukopenia induced by previous treatments by other agents, but repetition of the treatment is possible, if the polymorphonuclear leukocyte count is restored. The possibility of latent damage to the hemopoietic system should be borne in mind; this was illustrated by the fate of one of the dogs given a second treatment and by the serious leukopenia that occurred in one of the cases of Hodgkin's disease after a second small dose. In chronic leukemia the drug has been administered at a lower level of 0.1 to 0.2 mg. per kilogram and has been repeated at intervals of several weeks for maintenance. The response of cases of lymphoid leukemia has been better than that of the myeloid cases. This finding has been encouraging, since with most other therapeutic agents the response of lymphoid leukemia has been less favorable than that of myeloid leukemia. Functional tests and postmortem examinations have not revealed changes in the kidneys or liver after treatment. The hemopoietic system is highly sensitive to triethylene melamine. Although the oral administration of enteric-coated tablets seems a simplification, it involves the danger of being used without the essential hematological controls.

Bull. World Health Organ., Geneva

7:111-230 (No. 2) 1952. Partial Index

Epidemiological Factors in Tuberculosis Control: Observations on Distribution of Tuberculosis Mortality in Seven Countries. J. B. McDougall.—p. 111.
Tuberculin Sensitivity of Tuberculous Patients. C. E. Palmer and L. E. Bates.—p. 171.
BCG-Vaccine Studies: 5. Field Studies of Significance of Dead Bacilli in BCG Vaccine. S. N. Meyer and C. E. Palmer.—p. 201.

Deutsche medizinische Wochenschrift, Stuttgart

78:1-52 (Jan. 2) 1953. Partial Index

Current Treatment of Coronary Infarction. P. Uhlenbruck.—p. 1.
Experimental Bases of Effect of Repository Circulatory Hormone Preparation ("Padutin"). E. K. Frey and W. Hartenbach.—p. 5.
Treatment of Edema with Cation Exchange Resins. H. Herken.—p. 8.
*Effect of Visammin in Treatment of Angina Pectoris. K. Uhlenbroock.—p. 12.
*Visammin in Angina Pectoris and Bronchial Asthma. H. Brügel and H. Henne.—p. 14.

Visammin in Angina Pectoris.—Experimental animals were given 50 mg. of visammin (khellin) per kilogram of body weight. Within 24 hours of the injection, the amounts of visammin contained in the heart, lung, stomach, small intestine, liver, gallbladder, kidney, brain, and skeletal muscles of the animals were determined. The visammin content of the various organs varied considerably, the heart showing by far the highest content and maintaining its content much longer than the other organs. These observations indicate that visammin exerts its effect not only on the smooth muscle cells but also on the muscle fibers of the heart. The function of visammin in cell metabolism was studied with the aid of Warburg's apparatus. Results showed that visammin acts through a redox reaction, and it is, therefore, of great significance for cellular respiration, particularly in the anoxemic, impaired heart. This may explain the observation that tolerance to strophanthin may be restored occasionally in man by administration of visammin. According to the author, contraindications to the treatment with visammin had not been reported in the foreign literature. The property of visammin to act as a spasmolytic agent in the coronary region and possibly as a respiratory catalyst in the metabolism of the cardiac muscle makes it unlikely that visammin in therapeutic doses may have notable undesirable side-effects. By combining 20 mg. of visammin with 280 mg. of sodium salicylate, a satisfactory solution for parenteral administration was obtained. At the surgical clinic of the university in Hamburg, 10 ampuls of this solution (i. e., 200 mg. of visammin plus 2,800 mg. of sodium salicylate) were administered in the course of one operation on the cardiac muscle without any untoward reaction. Thirty additional heart operations were similarly performed without a single operative death. In two patients with latent tetany, the injection of the visammin and sodium salicylate solution

elicited a spasmodic disturbance apparently because of the ion exchange between the sodium salicylate and the calcium ions of the blood. The spasms subsided immediately after an injection of calcium. Venous pain was occasionally observed after the injection of the visammin solution, but this disturbance may be prevented by a combination of the visammin and sodium salicylate solution with polysaccharides or dextrose. Intramuscular injections of the visammin and sodium salicylate solution combined with 1 cc. of 1% procaine hydrochloride may be given without production of pain if intravenous administration is not possible. To prevent gastrointestinal disturbances, patients should not be given orally more than 40 to 80 mg. of visammin daily, and that only after meals.

Visammin in Angina Pectoris and Bronchial Asthma.—Visammin (khellin) with sodium salicylate used as solvent was given intravenously to 49 patients with angina pectoris and to 22 patients with bronchial asthma. As a rule the drug was given in doses of 20 mg. twice a day, but occasionally 40 mg. was given twice a day, and one patient with a recent infarct of the posterior cardiac wall was given 40 mg. three times a day. Of the 49 patients with angina pectoris, 20 obtained excellent results for prolonged periods, with significant relief or complete disappearance of pain shortly after the injection; 18 obtained good results that were of shorter duration; and 11 patients were therapeutic failures. It seems noteworthy that better results were obtained in patients with angina pectoris of severe or moderate degree than in those with angina pectoris of mild degree. Some of the patients also showed improvement of the previous abnormal electrocardiographic recordings. Although visammin was used primarily for symptomatic treatment because of its analgesic effect, its use for the elimination of the cause of angina pectoris seems to be suggested by its spasmolytic effect on the reflex spasms of the collateral vessels. Four of the 22 patients with bronchial asthma were definitely improved, 7 obtained moderate improvement, 8 were therapeutic failures, and results were doubtful in 3. The authors believe that visammin is more suitable for treatment of acute attacks of asthma or of status asthmaticus rather than for prolonged treatment of bronchial asthma. There were fewer untoward reactions to the drug than have been reported by other workers, probably because of the lower dosage, the exclusively parenteral administration, and the adequate solvent used. A sudden drop in blood pressure occurred in three patients, perhaps because of too rapid injection of the drug, but was controlled rapidly by oral administration of a proprietary preparation of synephrin® (*p*-hydroxyphenylmethylaminoethanol) tartrate.

Journal Obst. & Gynaec. Brit. Empire, Manchester

59:753-920 (Dec.) 1952

Fibromuscular Structure of the Cervix, and its Changes During Pregnancy and Labour. P. E. Hughesdon.—p. 763.
Liver Cirrhosis and Pregnancy. R. W. Burslem, C. Gardikas and M. C. G. Israels.—p. 777.
Parovarian Carcinoma: Hitherto Undescribed Tumour. B. Lennox and D. J. Meagher.—p. 783.
Antepartum Haemorrhage. D. Murdoch and J. F. Foulkes.—p. 786.
Rupture of the Spleen in Pregnancy: Review of Recorded Cases with Further Case Report. T. Barnett.—p. 795.
Severe Intraperitoneal Bleeding in Latter Half of Pregnancy: Case Report. J. Henderson and D. M. W. Maxwell.—p. 803.
Review of 115 Cases of Postmaturity. G. Hill.—p. 807.
Renal Agenesis. G. Allen and N. P. Orchard.—p. 810.
Surgical Induction of Labour: Survey. G. B. Gibson.—p. 814.
Pregnancy Complicated by Congenital Polycystic Disease of the Kidneys. N. Morris.—p. 822.
*Role of Trauma in Aetiology of Abortion. H. J. Whiteley and H. N. Green.—p. 829.
Case of Primary Carcinoma of Fallopian Tube Associated with Tuberculous Salpingitis. W. P. G. Dickson, K. V. Lodge and A. S. Woodcock.—p. 834.
Rupture of Myomectomy Scar During Pregnancy. J. E. Mackie.—p. 838.
Logical Treatment of Breech Presentation. G. Dalley.—p. 841.

Role of Trauma in Etiology of Abortion.—It has long been believed that a fall or some injury sustained during pregnancy may result in abortion or premature delivery. Some investigators have indicated that adenosine triphosphate and adenine nucleotides might play a role in the bodily response to injury, and so the observation by one of the present authors that the injection of adenosine triphosphate into the pregnant rat caused uterine contractions was of considerable interest. In view of this observation and the somewhat conflicting reports on trauma as a factor in abortion, it was decided to investigate the effect of adenosine triphosphate on the course of pregnancy in rats and rabbits and on the isolated human uterine muscle. Adenosine triphosphate was found to cause contraction in the isolated uterine muscle of rats, rabbits, and women. The sensitivity of the uterine muscle increased with advancing pregnancy. In the intact rabbit intravenous administration of adenosine triphosphate produced uterine contractions in the virgin animal and during early pregnancy. Intravenous administration of epinephrine produced a response similar to adenosine triphosphate. Interruption of pregnancy occurred in three of four rabbits during early gestation; in two of these four muscle ischemia had been induced, and in two 200 mg. of adenosine triphosphate had been injected intramuscularly. The human uterus is known to react to epinephrine in a manner similar to the reaction of the rabbit uterus. The experimental evidence thus supports the view that tissue injury or psychic shock in the early stages of human pregnancy might cause uterine contractions by the liberation of epinephrine and thus dislodge an already damaged embryo or possibly even expel a normal embryo.

Lancet, London

1:53-102 (Jan. 10) 1953

*Geographic Variation in Naturally Acquired Tuberculin Sensitivity. L. B. Edwards and C. E. Palmer.—p. 53.
Gout, Leukaemia, and Polycythaemia. R. A. Hickling.—p. 57.
Supportive Therapy: Improved Type of Dextran. A. M. Boyd, F. Fletcher and A. H. Ratcliffe.—p. 59.
Rejection Dyspepsia. G. G. Robertson.—p. 63.
Urinary Excretion of Pepsinogen in Gastroduodenal Ulceration. B. I. Hirschowitz.—p. 66.
Mumps Orchitis Without Parotitis in Infants. N. K. Connolly.—p. 69.
Modified Schlesinger Test for Urobilin in Urine. H. F. W. Kirkpatrick.—p. 71.
*Cortisone and Liver Function. K. Aterman and N. D. Ahmad.—p. 71.

Variations in Naturally Acquired Tuberculin Sensitivity.—The patterns of tuberculin sensitivity found before BCG vaccination of children in Denmark, Mexico City, Egypt, and South India are presented. Histograms of reactions to weak doses (5 or 10 tuberculin units) on sizable samples of children in these four countries reveal that there are three degrees of tuberculin sensitivity: high-grade sensitivity (strong reactions), low-grade sensitivity (small reactions), and relative nonsensitivity. High-grade sensitivity represents the specific response to contact and infection with human tuberculosis in the classical sense. Low-grade sensitivity, on the other hand, seems to be independent of true tuberculous infection but closely associated with geographic factors. The third kind is present in children who have neither had a tuberculous infection nor have been subjected to the influence of the unknown factor that causes low-grade sensitivity. There are wide variations in different countries in the proportion of children having each of the three different kinds of sensitivity. The present system of selecting children for vaccination (according to the size of the reaction to a weak dose of tuberculin) seems to be fairly satisfactory for assuring that those with a high level of allergy will not be vaccinated. But it is entirely inadequate for separating children with low-grade sensitivity either from those with high-grade sensitivity or from those who are nonsensitive to tuberculin. By the present scheme some children with low-grade sensitivity are vaccinated and some are not. This seems illogical. It also emphasizes the unexpected pitfalls when techniques and procedures are directly transplanted from one country to another without prior knowledge of the differences that may exist in different parts of the world.

Cortisone and Liver Function.—Since the amount of fibrous tissue deposited in the liver of rats given carbon tetrachloride is reduced if cortisone is administered simultaneously, it seemed of interest to ascertain whether this neutralizing effect is associated with a corresponding change in the function of the liver. Twenty-three albino rats were given 21 subcutaneous

injections of 0.2 cc. of carbon tetrachloride at intervals of two or three days; the rats were of an inbred stock and were fed a stock laboratory diet. After the 17th injection, the rats were starved for 16 hours and the sulfobromophthalein (bromsulphalein®) test was made. Next day treatment with cortisone was started in 12 of the rats, the remainder being kept as controls. Cortisone acetate was given intramuscularly in two divided doses, the daily dose being 12.5 mg. on the first and last day and 10 mg. and 8.75 mg. alternately for the rest of the experiment. Each rat received a total of 90 mg. The injections of carbon tetrachloride were continued in both groups during the time the one group received cortisone. After the last injections of both carbon tetrachloride and cortisone, the rats were again starved for 16 hours and the sulfobromophthalein test was repeated. It was found that cortisone has little effect on sulfobromophthalein retention in the normal rat, but produces considerable deterioration if given to rats treated with carbon tetrachloride for seven weeks. The histological picture showed more widespread liver damage in these rats than in a control group treated only with carbon tetrachloride. Cortisone increases the susceptibility of the rat's liver to chronic damage by carbon tetrachloride.

Medical Journal of Australia, Sydney

2:801-832 (Dec. 6) 1952

Acute Mastitis: Study of 28 Cases. C. Isbister.—p. 801.
New Excursion into Ether Anaesthesia. R. B. Lynch.—p. 808.
Facial Paralysis: Clinical Review with Autopsy Report of Histo-Pathology in Case of Infection of Geniculate Ganglion by Virus of Cephalic Herpes Zoster. J. P. Findlay.—p. 810.

2:833-872 (Dec. 13) 1952

Tuberculosis in Childhood, as Disclosed or Confirmed by Cultivation of Mycobacterium Tuberculosis from Gastric Content. R. Webster.—p. 833.

2:873-896 (Dec. 20) 1952. **Partial Index**

Mass Management of Burns: Civil Defense Aspect. S. Burston.—p. 873.
Id.: Resuscitation. R. J. Walsh.—p. 878.
Laboratory Aspects of Mass Management of Burns. J. W. Perry.—p. 880.

Minerva Medica, Turin

43:1141-1172 (Nov. 26) 1952. **Partial Index**

Dihydroergotamine and Neuroregulation of Carbohydrates Metabolism in Man. A. G. B. Lusso.—p. 1146.
Antiheparin Effect of Vitamin E in Vitro and Its Action Enhancing Thromboplastic Activity of Plasma. F. De Matteis and C. Marenzana. —p. 1152.
*Co-carboxylase in Treatment of Diabetic Acidosis and Some Diabetic Complications. R. Klinger and P. Dalle Coste.—p. 1158.

Cocarboxylase in Diabetic Complications.—Cocarboxylase ("bioxilase") was used intramuscularly to treat 62 patients with diabetes in whom complications had developed. Thirty-six had acetonuria, 15 neuritis, 4 paresis, 5 retinopathy, 1 psoriasis, and 1 severe asthenia. The dose, proportional to the severity of the complication, ranged from 25 mg. to 100 mg. daily for 3 to 50 days. For a more objective evaluation of the activity of the drug, the diet and the insulin doses were not modified. Results were gratifying in 83.3% of the patients. In only one patient with acetonuria and one with asthenia the treatment had to be interrupted because pain and paresthesia developed in the extremity where the drug had been injected. One patient with acetonuria in whom all previous antiketonic treatment had failed showed marked improvement, and acetone was not seen in his urine for several days. Pronounced improvement was also observed in the hyperglycemia and the glycosuria of another patient with acetonuria. The five patients with retinopathy who were still undergoing treatment at the time of writing improved greatly subjectively; there was also a slight improvement in the fundus oculi. One patient with almost total ptosis of the right upper lid recovered completely after 30 days. Although the condition of the patients regresses to its initial phase after the treatment is interrupted (as is the case with insulin therapy), this does not attenuate the value of this drug, since it can be given in cycles, and seems to have a tonic effect, particularly in patients with asthenia.

Monatsschrift für Kinderheilkunde, Berlin

100:457-496 (Nov.) 1952

Pathological-Anatomic Study of Clinical Types of Diphtheria. U. Genz. —p. 462.
Prevention of Jarisch-Herxheimer Reaction in Penicillin Therapy of Congenital Syphilis. K. Seelemann and B. Kornatz-Stegmann.—p. 472.
*Epidemic Occurrence of Bornholm Disease in Children. H. Prenzel. —p. 475.
*Lambliasis as Cause of Obscure Abdominal Pains and Liver Disease in Children. K. Daecke.—p. 479.

Outbreak of Epidemic Pleurodynia.—Early in the fall of 1951 an outbreak of epidemic pleurodynia (Bornholm disease) occurred in a region of northwestern Germany. Most of the patients were children. In some cases several children in the same family became ill one after the other, and numbers of children in the same classrooms were sometimes affected. This author made clinical observations on 19 children ranging in age from 2 to 14 years, and observed a number of others in the ambulatory service. The symptoms were usually like those of an attack of influenza of moderate severity, with elevation of temperature, headache, vomiting, meningism, and the very typical lancinating pains in chest and side (pleurodynia). Meningitis with myalgia often was the most outstanding symptom in those requiring hospital treatment; it often appeared during the second phase of the disease. The differentiation of epidemic pleurodynia from poliomyelitis, leptospirosis, and other forms of "serous meningitis" and the results of virologic examinations are discussed. The virus apparently belongs to the Coxsackie group of viruses.

Lambliasis as Cause of Abdominal Pains and Liver Disease in Children.—Recurrent abdominal pains accompanied by impairment of the general condition often present a diagnostic problem to the pediatrician. Helminthiasis, relapsing pyuria, tuberculosis of the mesenteric lymph nodes, gastritis, duodenal and gastric ulcer, chronic appendicitis, congenital anomalies of the abdominal organs, lithiasis, hernias, and cardiac disorders are among the disorders that must be ruled out. Latent liver disease, although usually recognized in adults, is often overlooked in children. Daecke stresses that latent infection with Giardia (Lamblia) intestinalis may sometimes be the cause of liver disease in children. With the aid of duodenal aspiration, G. intestinalis is readily detectable in the warm duodenal contents, the pear-shaped protozoan with two nuclei and eight flagella being highly motile. Warm diarrheal stools may yield the protozoan flagellates; and air-dried, bile sediment stained with Giemsa stain may also permit identification of the Giardia organisms. The author reviews observations on seven children with latent liver disease in whom the etiology of abdominal pains was at first obscure. They could be traced to infection with G. intestinalis. The abdominal pains had in some cases existed for more than a year. Daecke differentiates an intestinal (enterocolitic), and a hepatic or hepatocholepathic form of lambliasis, and a form with generalized symptoms. The abdominal pains are caused by irritation and inflammation in the gastrointestinal tract, particularly in the duodenum and the bile passages. The improvement that followed treatment with quinacrine (atabrine®) hydrochloride is proof of the pathogenetic role of the Giardia organisms. Treatment with quinacrine hydrochloride is usually continued for five days, the daily doses being the same as when the drug is used in the treatment of malaria. After an interval of 14 days, the drug may be given for 3 more days. If the first five day treatment should fail, a second or third course may be given.

Philippine Medical Association Journal, Manila

28:637-682 (Nov.) 1952

Sensitivity and Specificity of Three Laboratory Procedures for Serological Test for Syphilis. A. P. Roda and F. Catanjal.—p. 637.
Personal Experience with Chloromycetin in Typhoid. F. R. Pascual. —p. 645.
Classical Type of Chronic Familial Hemolytic Anemia in the Philippines. E. Stransky and D. F. Dauis-Lawas.—p. 647.
Health Hazards in Chromium Plating: Survey of Some Establishments In and Around Manila. G. D. Dizon, J. Anselmo, V. Luciano and others. —p. 651.

Practitioner, London

170:1-104 (Jan.) 1953. **Partial Index**

What is Indigestion? T. J. Horder.—p. 6.
Neuroses as Seen by Gastroenterologist. W. C. Alvarez.—p. 10.
Peptic Ulcer Dyspepsia. G. D. Hadley.—p. 18.
Indigestion as Manifestation of Cancer of the Stomach. J. Bruce.—p. 27.
Gall-Bladder Dyspepsia. R. E. Tunbridge.—p. 33.
Constipation and Indigestion. J. F. Dow.—p. 39.
Alcohol, Dietetic Indiscretion, and Dyspepsia. W. G. Sears.—p. 43.
Indigestion as Symptom in Systemic Disease. H. K. Goadby.—p. 51.

Praxis, Bern

41:1121-1140 (Dec. 26) 1952

Unrecognized Fracture of Tibia in Small Child and Diagnosis. E. Gardaz. —p. 1122.
*Further Clinical Observations with Total Cardiac Extract "Recosen"; Second Report. S. Greif.—p. 1125.
New Contribution to Treatment of Bronchial Asthma. N. Belli.—p. 1128.

Clinical Experience with Total Cardiac Extract.—Satisfactory results in 60 patients obtained with "recosen," a protein-free extract of the entire animal heart, were reported by the author in a previous paper. These good results prompted a therapeutic trial of the preparation in an additional 103 patients. In 26 patients with decompensated myocardial lesions and an increased tendency to extrasystoles (bigeminal and trigeminal pulse), the extrasystoles disappeared and a normal rhythm was restored by combined intramuscular and oral administration of "recosen" for 8 to 10 days. The same favorable results were obtained in patients in whom the tendency to extrasystoles represented a toxic side-effect of prolonged treatment with digitalis preparations, as well as those in whom the extrasystoles resulted from organic cardiac disease. Pain and nocturnal dyspnea disappeared almost completely in 43 patients with less severe myocardial lesions, but the decompensation did not subside. In 34 patients with severe angina pectoris who were given a four week course of treatment with two intramuscular injections of 1 cc. of "recosen" and three tablets orally per day, complete or nearly complete relief from the agonizing constant sense of pressure was obtained within 16 days. The severe attacks subsided completely or became less frequent and less severe, and in some of the patients the improvement was also revealed by the electrocardiogram. The author concludes that "recosen" is a valuable adjuvant in the treatment of cardiac diseases and is of great importance in the treatment of angina pectoris.

Presse Médicale, Paris

60:1699-1718 (Dec. 17) 1952. **Partial Index**

Natural and Artificial Hibernation of Hibernators and Experimental Generalized Hypothermia of the Rat and Certain Hibernators. C. Kayser and H. Hiebel.—p. 1699.
Studies on Diabetic Ketosis and Acidoketosis: II. Reflections on Two Cases of "Diabetic Coma" (Severe Diabetic Acidoketosis). E. Azerad, H. Lestradet and D. Alagille.—p. 1702.
*Artificial Hibernation by Laborit Method. A. Bobbio, P. Goffrini and E. Bezzi.—p. 1708.

Artificial Hibernation.—The two basic elements of artificial hibernation are the blocking of the vegetative nervous system with drugs and the reduction of the basal metabolism by refrigeration of the patient with ice bags covering a large part of the body. The decline in the metabolism is accompanied by diminished cardiac and circulatory activity. The vegetative blocking alone may be used for therapeutic purposes, because it induces somnolence and potentiates the action of the customary anesthetics, greatly reducing the amount required to produce narcosis. Refrigeration, on the contrary, cannot be used alone, because the application of cold to an extensive surface of the body will provoke a defensive reaction unless the patient has been rendered unresponsive. The procedure is highly efficacious, but the indications for its use are at present limited to conditions in which the body is exhausted and the operation to be undertaken is severe, as in cases of cancer, intestinal stenosis, and generalized peritonitis. Total hibernation was used for 10 patients, aged from 53 to 74 years, who were in poor condition and who were subjected to such major surgical procedures as subtotal gastrectomy, splenectomy, disarticulation of the shoulder, and appendectomy for appendiceal gangrene. Refrigeration was started during the operation with the symmetrical and successive application of ice bags to the popliteal, inguinocrural, and antecubital regions, the axillas, the feet, and finally the precordial region. Administration of the autonomic blocking agents was continued because without them the refrigeration was not tolerated. The temperature usually fell from the first hour on, finally becoming stabilized at from 32 to 34 C, where it should remain throughout the period of hibernation. The pulse and blood pressure levels were generally normal; when hypotension was observed, the normal level was regained gradually within seven or eight hours. Hibernation was continued for about 48 hours, after which the ice bags were withdrawn progressively in inverse order and the doses of the autonomic blocking agents were gradually reduced, until the patient recovered warmth and the temperature returned to normal. All the patients were not only clinically cured but had a smooth postoperative course without complications. Experiments on dogs have shown that artificial hibernation affords protection from primary neurogenic shock and leads to a reduction in thyroid function that ends when the treatment is discontinued. These findings help to explain the efficacy of artificial hibernation and may broaden the indications for its therapeutic use.

Rev. Asociación Médica Argentina, Buenos Aires

66:299-334 (Aug.-Sept.) 1952. **Partial Index**

World Medicine and Industry. R. Collier.—p. 300.
Actual Prognosis and Treatment of Tuberculous Meningitis in Laënnec Hospital. E. Bernard.—p. 304.
*Verrugoma of Gougerot (Granuloma Pyogenicum) Therapy. J. M. Spilzinger.—p. 315.
Carcinoma of Breast of Comedo Type. M. F. Couretot and J. Mayo. —p. 319.

Treatment of Granuloma Pyogenicum.—The author reports the cure of a large granuloma pyogenicum following the injection into the base of the lesion of 300,000 units of sodium penicillin and 0.5 cc. of a 5% procaine (novocaine®) solution in 1 cc. of distilled water. The lesion was a hemispherical tumor appearing on the cheek of a 50-year-old woman and growing within four months to a diameter of 3 cm. Clinically it had features of both granuloma pyogenicum and epithelioma, but its disappearance within two weeks after the penicillin injection ruled out the latter diagnosis. A superficial erosion remained after the tumor disappeared, but this was cleared up within a few days with an ointment containing ichthyol and yellow oxide of mercury. There has been no recurrence in six months. The treatment is painless, does not produce local complications, is followed by rapid cure, and does not produce scars.

Scandinavian J. of Clin. & Lab. Investigation, Oslo

4:251-378 (No. 4) 1952. **Partial Index**

*Some Aspects of Clinical Physiology of Noradrenaline. U. S. von Euler. —p. 254.
*Adrenaline and Noradrenaline in Blood and Urine in Cases of Pheochromocytoma. A. Lund.—p. 263.
ECG-Changes Seen in Cases of Pheochromocytoma Compared with Changes Experimentally Evoked by Adrenaline. P. Cannon and T. Sjöstrand.—p. 266.
Effect of Adrenaline and Noradrenaline on Carbohydrate Metabolism of Rat Diaphragm. E. Walaas and O. Walaas.—p. 268.
On Paper Electrophoresis in Clinical Laboratory. A. Grönwall.—p. 270.
Experiences with Antweiler's Micro-Electrophoresis Apparatus. E. Bierring and E. Nielsen.—p. 281.
Paper Electrophoresis in Diagnosis of Liver and Bile Duct Diseases. G. Brante.—p. 293.
Reproducibility with Paper Electrophoresis of Serum Proteins. S. C. Sommerfelt.—p. 307.

Physiological Effect of Arterenol.—The circulatory effects of arterenol are briefly reviewed. Arterenol proved to be an effective and safe therapeutic agent in postoperative and other forms of shock, spinal anesthesia, myocardial infarcts, and various intoxications causing circulatory collapse. Studies on the urinary excretion of arterenol showed that it is increased in cases of chromaffin cell tumors, in heavy muscular exercise, in some cases of essential hypertension, and in coronary

thrombosis. Increased epinephrine excretion was observed in adrenal medullary tumors, hypoglycemia, and in various conditions involving stress. Observations on patients who were subjected to adrenalectomy showed that the epinephrine is chiefly derived from the adrenal medulla and the arterenol from the adrenergic nerve endings. The evidence to date indicates, generally speaking, that arterenol maintains the homeostasis of the circulatory system, whereas epinephrine is secreted by the organism in response to various forms of stress.

Epinephrine and Arterenol in Patients with Pheochromocytoma.—Blood samples taken from persons with normal blood pressure or from patients with hypertension when their blood pressure was nearly normal did not contain detectable amounts of epinephrine or arterenol. Similarly, these substances were not present in blood obtained from seven patients with essential hypertension. In five additional patients with paroxysmal hypertension, readily detectable amounts of arterenol were observed in blood samples taken during an attack, and in four of these patients the diagnosis of pheochromocytoma was confirmed by the removal of a tumor containing arterenol. Although venous blood does not normally contain detectable amounts of epinephrine or arterenol, small but significant amounts of these amines are excreted in the urine. The author's patients with pheochromocytoma excreted 10 to 100 times as much pressor amines as normal persons. The pressor amine content, especially arterenol, in some of the removed pheochromocytomas, was found to be very high as compared with that in normal adrenal glands. As a result of his observations, the author states that, if venous blood from patients with hypertension contains 1 μg per 100 cc. or more of epinephrine or arterenol, it strongly indicates the presence of a pheochromocytoma. Concentrations of pressor amines in the urine higher than 10 μg per 100 cc. are pathological. If the 24 hour excretion essentially exceeds 100 μg of arterenol (plus epinephrine), it is highly probable that the hypertension is caused by a pheochromocytoma.

Schweizerische medizinische Wochenschrift, Basel

82:1325-1348 (Dec. 27) 1952. **Partial Index**

*Treatment and Prognosis of Chronic Morphinism. P. Kielholz.—p. 1325.
Treatment of Carcinoma of Female Sex Organs; Statistical Report. G. Reichen and H. Erb.—p. 1329.
Percutaneous Absorption of Desoxycorticosterone and Cortisone. W. Jadassohn, E. Bujard, R. Paillard and G. Adé.—p. 1331.
Chemical Effect of Cosmic Rays. J. Eugster and L. Jenny.—p. 1332.
*Postoperative Fatal Circulatory Collapse After Treatment with Oxytetracycline ("Terramycin"); Case Histories. F. Meier.—p. 1337.

Chronic Morphinism.—As a result of his observations on 50 patients with chronic morphinism, the author prefers the sudden and immediate withdrawal to slow or gradual withdrawal of morphine as well as to rapid withdrawal of the drug within one to two weeks. The two methods for the sudden withdrawal of the drug are treatment by continuous sleep or by insulin therapy. The author prefers insulin therapy because it does not entail a refractory prolonged disturbance of sleep, as continuous sleep therapy does. The insulin therapy consists of three injections of individual doses of insulin (20 to 80 units) given at 7 a. m., 2 p. m., and 8 p. m. daily for 10 days. At the end of each of the three daily insulinization periods the patient is given orally dextrose in tea, and at the end of the second insulinization period a warm bath of half an hour duration. Thus natural sleep may result spontaneously from the sedation of the entire nervous system. In still refractory patients, a calcium bromide effervescing powder may be used for the induction of sleep, or 20 to 30 drops of dihydroergotamine may be given to patients with signs of predominantly sympathetic irritation. After 10 days of insulin therapy, treatment may be continued with one injection of insulin at 8 p. m. daily for three to five weeks. The first 10 days of treatment should be used to establish a relationship of profound confidence between the addict and the physician. Only after morphine withdrawal has been accomplished should the study of the patient's character and of the motives of his addiction as well as psychotherapy be instituted. By treating the conscious and unconscious causes of his addiction psychologically, the addict should become a person who is able to cope with reality. After discharge from the hospital, psychotherapy should be continued ambulatorily for two to three years to prevent recurrences. Of the author's 50 patients, 37 had a hereditary character defect with hypersensitiveness and want of willpower and a tendency to depression and hysteria. In only 11 addicts was a permanently painful physical disease the motive of the addiction, while in the other 39 the addiction was due to mental causes. Follow-up of these 39 patients for at least one year after their discharge from the hospital revealed that 15 (38%) had become definitely free of their addiction, while results were doubtful or recurrences had been observed in the remaining 24 (62%). The prognosis of morphinism due to an underlying physical disease depends on effective treatment of this disease, while the prognosis of morphinism due to mental causes depends on the hereditary defect, the physical and mental constitution and the social constellation, and to a much lesser degree on the duration and the number of recurrences. In contrast to other workers, the author considers the prognosis more favorable in men than in women. The urgent need for stricter control of the dispensing of analgesics and soporifics is suggested by the fact that in 30 (60%) of the author's patients morphinism was associated with the abuse of milder analgesics and barbiturates and that recurrences of this abuse were observed in 8 (16%).

Fatal Postoperative Circulatory Collapse After Oxytetracycline Therapy.—Death from circulatory collapse occurred within seven days after laparotomy for diseases of the colon in three patients aged 47, 54, and 60 years. Preoperatively and postoperatively all three patients had been given oxytetracycline ("terramycin") orally in daily doses of 1.5 gm., with a total dose of 3 to 6 gm. Surgical intervention was performed with the patient under nitrous oxide and ether anesthesia and without any disturbance. The postoperative course first was normal, with spontaneous restoration of the function of the intestines in the absence of any circulatory disturbance. Diarrhea occurred on the third to the fifth postoperative day and was followed by sudden circulatory collapse that was refractory to all therapeutic procedures and resulted in death within 48 hours. Similar observations were made by American workers in patients treated with oxytetracycline in whom the occurrence of fatal collapse was considered the result of superinfection by staphylococci after disappearance of the normal intestinal flora. A cause-and-effect relationship between the observed postoperative fatal complication and the treatment with oxytetracycline has been postulated likewise by the author in his cases.

Semaine des Hôpitaux de Paris

29:1-46 (Jan. 2) 1953

Effect of Intraspinal Tumors on Bones. T. Alajouanine, R. Thurel and Hasaerts.—p. 2.
Tuberculous Fibrous Leptomeningitis. R. Thurel.—p. 8.
*Occurrence of Cysts in Cerebral Tumors. R. Thurel.—p. 12.
Thrombophlebitis of Vein of Galen: Hemorrhages Into Central Gray Nuclei and Pineal Body. R. Thurel, J. Pedrono and J. Gruner.—p. 17.

Occurrence of Cysts in Cerebral Tumors.—According to Thurel, the occurrence of cysts in a cerebral tumor, whether it is a glioma or a hemangioma, should be considered an active phenomenon rather than a degenerative process. If there is a retrograde change in the tumor, it occurs subsequent to the production of fluid under pressure and to the shrinking of the neoplastic tissue. Such an involution may progress toward the complete extinction of the neoplastic process. The occurrence of a cystic glioma in a 15-year-old girl and of a cystic astrocytoma in a 50-year-old man is reported. Removal of the mural tumor and of the wall of the cyst in the girl did not prevent the recurrence of the tumor after five years. Whereas the primary tumor had a central islet of glial tissue poor in cells indicating a limited activity, the recurrent tumor showed in one section of its peripheral area ependymal cavities filled with a fluid rich in fibrin and everywhere else a thick peripheral fringe with spongioblasts surrounding the vessels. In the male patient the anterior pole of the frontal lobe was removed with the cystic tumor, but a poorly limited infiltrative tumor consisting of spongioblasts situated around the vessels re-

curred after two years. The tendency to recurrence and particularly to recurrence in a more differentiated form despite thorough removal of the primary tumor induces the author to recall a case of cystic glioma of the left temporal lobe reported by him and several co-workers in 1930; a 10 year cure was obtained by simple puncture for the purpose of aspirating the accumulated fluid, followed or not by temporary injection of a modifying fluid such as alcohol. The possibility of involution of the tumor resulting from the cystic process with disappearance of all histological characteristics must be considered.

Tubercle, London

34:1-32 (Jan.) 1953

Use of INH in Pulmonary Tuberculosis. O. Düggeli and F. Trendelenburg.—p. 2.
Isoniazid in Treatment of Pulmonary Tuberculosis. D. M. Collins and D. A. L. Bowen.—p. 8.
Isonicotinic Acid Hydrazide in Pulmonary Tuberculosis. K. M. Martischnig and P. M. Ward.—p. 14.
Case of Pulmonary Histoplasmosis. A. Sakula.—p. 18.
Tuberculin-Sensitivity Among Child Contacts in Leeds, 1948-1949. J. Aspin and K. H. M. Lotinga.—p. 20.
An Unusual Case of PAS Allergy. B. Mann.—p. 23.

Ugeskrift for Laeger, Copenhagen

114:1751-1784 (Dec. 4) 1952

*Cancer of Lungs: I. Symptomatology and Diagnosis. F. Heintzelmann.—p. 1751.
*Id.: II. Possibility for Early Diagnosis. F. Heintzelmann.—p. 1756.
*Id.: III. Summary of Diagnostic Problems. F. Heintzelmann.—p. 1760.
*Radical Treatment of Cancer of Lungs. F. Therkelsen and H. R. Sørensen.—p. 1761.
Eating Problems in Childhood. S. Frandsen and P. Jacoby.—p. 1765.
Liposarcoma of Humerus Treated by Excision and Acryl Prosthesis. J. Agerholm-Christensen.—p. 1768.

Cancer of Lungs.—Heintzelmann says that, of 87 patients with pulmonary cancer treated in Frederiksberg Hospital from 1946 to 1951, 80 are dead; most of the patients were men between the ages of 55 and 64 years. In two-thirds of the cases death occurred within the first half year after admission. In 45 cases the diagnosis was made within half a year after onset of the symptoms. Two-thirds of the patients were admitted with other diagnoses. The symptoms resembling those of cardiac disease are stressed. The roentgen picture was abnormal in all cases. Tumor cells were demonstrated in only a few cases. The diagnosis was verified during life in 38 cases, in 20 by bronchoscopy and in 9 by exploratory thoracotomy. Metastases on admission were found oftenest in younger patients, and fatal cases without metastases occurred almost exclusively in old, inoperable patients. Sixteen patients were operated on, but the tumor could be removed in only seven, in 3 of the 33 patients under 65 having symptoms for less than half a year and in 4 of the 21 also under 65 having symptoms for more than half a year. In six of these cases the history suggested cancer of the lungs, and in the seventh a chance stethoscopic finding led to suspicion of cancer. From 1948 to 1950 201 patients out of 4,700 admitted under diagnoses other than pulmonary cancer were observed for possible pulmonary cancer because of suspicious symptoms. After continued examinations and observation, cancer of the lungs was diagnosed in 10% of the patients. Cancer of the lung was found in many patients admitted for heart disorder. No patient with completely normal roentgenogram of the lungs had pulmonary cancer. Unsuspected cancer of the lungs was found in two of the remaining 4,500 patients. The six main symptoms of bronchogenic carcinoma are cough, expectoration, dyspnea, pain in the chest, loss of weight, and exhaustion, with frequency in the order named. The symptoms were present in from one-half to two-thirds of the cases, but because of their nonspecific character the disease is easily misjudged at the start. The symptoms usually lead to admission within a half year after their onset. Only hemoptysis can be expected immediately to lead to correct diagnosis. Dyspnea should quickly awaken suspicion. Pulmonary cancer should be considered among the etiological possibilities in paroxysmal tachycardia, although it is a relatively rare symptom in the disease. An abnormal roentgen picture should be followed by bronchoscopy; if the picture is normal, bronchoscopy is considered necessary only in case of extremely suspicious symptoms. Clinical diagnosis of pulmonary cancer, i. e., diagnosis about half a year after start of symptoms, can not be made early enough, except for the few cases of tumors that grow slowly and metastasize late. Early diagnosis of pulmonary cancer is tantamount to diagnosis before the symptoms appear; cases in which successful operation can be expected are those discovered accidentally in mass roentgen examinations in tuberculosis stations and in more accidental roentgen examinations of the thorax. Bronchogenic carcinoma seems to develop so rapidly that it is impractical to depend on routine health examinations for its detection.

Radical Treatment of Pulmonary Cancer.—Therkelsen and Sørensen discuss the results of radical treatment of cancer of the lungs on the basis of percentage of operable lesions, operative mortality, and late results. Of their 351 cases of pulmonary cancer from the Rikshopital's thoracosurgical department from 1942 to 1951, 26.7% were operable. In their cases the operative mortality has decreased in the last two years to less than 15%. The decrease is due to progress in anesthesia, operative technique, and combatting of infection. Of 65 patients operated on radically and observed for at least three years, 23 were living at the time of writing. A close examination of these patients was under way; none of the seven that had already been examined had shown signs of recurrence or metastases, and six had wholly or in part resumed their usual work. The duration of survival in the inoperable cases was 5.4 months and for the patients operated on who died later 21.9 months.

Zentralblatt für Chirurgie, Leipzig

77:2431-2462 (No. 50) 1952

Cancer of Thyroid with Bone Metastases. H. Burmeister.—p. 2431.
Primary Sarcoma of Gallbladder. H. J. Raffauf.—p. 2437.
Pathological Changes in Mesenteric Lymph Nodes in Ascariasis. N. Zylka.—p. 2442.
Surgical Restoration of Rectal and Urinary Continence. H. Pröscher.—p. 2450.
*Importance of Prophylactic Alkalinization in Hypertrophy of Prostate. G. W. Heise.—p. 2455.

Prophylactic Alkalinization in Hypertrophy of Prostate.—Nephrogenic acidosis signifies the accumulation in the blood of aromatic and aliphatic acids as a result of impairment of the renal function. If the kidney loses its capacity to form ammonia, it is no longer capable of regulating the pH of the blood, and the alkali reserve of the blood has to serve for the neutralization of the nitrogen-containing acids. In patients with hypertrophy of the prostate the tubular apparatus of the kidney becomes damaged as the result of urinary stasis, so that it loses the capacity to concentrate the urine. A temporary compensatory polyuria is followed by an increase of the urea content and of the nitrogen-containing acids in the serum. The resulting reduction in the alkali reserve causes acidosis, which at first is latent but later results in true uremia. To counteract this acidosis Heise administered sodium bicarbonate orally in 10 gm. doses three times daily for four days. After such treatment the alkali reserve remained at about the same level for from 10 to 14 days, so that the effect of such medication outlasted the critical period during which the operation was performed. In many cases a second period of alkalinization was instituted after the operation. Nearly two-thirds of the patients with hypertrophy of the prostate, who had high urea values, had nephrogenic acidosis. Alkalinization reduced the period of preoperative treatment to an average of 14 days. Postoperative treatment as a rule did not exceed three weeks. Systematic alkalinization was induced in a total of 88 cases over the period of 12 months. Various surgical methods were used for the intervention on the prostate. The most frequently employed were Voelcker's ischiorectal approach and Millin's retropubic operation. Prophylactic alkalinization reduced the number of fatalities considerably. No patients died as the result of urinary sepsis. Prophylactic alkalinization as well as prophylactic antibiotic treatment should be used in patients with hypertrophy of the prostate.

BOOK REVIEWS

A Text-Book of Mental Deficiency (Amentia). By A. F. Tredgold, M.D., F.R.C.P., F.R.S., Consulting Physician to University College Hospital, London. Assisted by R. F. Tredgold, M.A., M.D., D.P.M., Physician to Department of Psychological Medicine and Lecturer in Medical School of University College Hospital, London. Eighth edition. Cloth. $7.50. Pp. 545, with illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1952.

The popularity of this textbook on mental deficiency is shown by the fact that it has gone through eight editions. This edition follows the plan of previous ones. The chapter on etiology has been rewritten to include recent work on prenatal pathology. Other chapters have been rewritten in part or otherwise brought up-to-date. The monograph is divided into 22 chapters covering all aspects of inherited and acquired mental defects. The role of inheritance and prenatal and postnatal factors in the genesis of mental deficiency are fully considered, and improbable causative factors are critically discussed. There is a brief but adequate description of all the common clinical syndromes that may be accompanied by mental retardation. Education, medicolegal, and sociologic aspects are well discussed. Forty-eight well-chosen figures illustrate various defects in the central nervous system and characteristic anomalies in the bodily structures of mentally deficient patients. A comprehensive index 15 pages long is included. References to the literature are numerous and are up-to-date. The volume is an excellent summary of the status of our knowledge of mental retardation and is of value to pediatricians, psychiatrists, and neurologists.

The Principles and Practice of Medicine: A Textbook for Students and Doctors. By L. S. P. Davidson, B.A., M.D., F.R.C.P., Professor of Medicine and Clinical Medicine, University of Edinburgh, and Staff of Department of Medicine and Associated Clinical Units. Cloth. $6.75. Pp. 919, with 58 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2; E. & S. Livingstone, Ltd., 16 and 17 Teviot Place, Edinburgh 1, 1952.

This compact book presents the lectures of a Scottish professor of medicine and his staff. It represents one compromise that is possible, and often very good, in writing a book that is beyond the scope of a single author. While most large textbooks published in the U. S. on internal medicine are now written by a number of authors who are geographically separated, this book represents the advantages of the authors being a closely knit group. It surveys the field of internal medicine and includes incidental consideration of pediatrics, psychiatry, and infectious disease.

Although the presentation of each disease is quite succinct, each is still readable. Because of this, the book may have a special use as a simple orientation and introduction to the field of internal medicine that is lost in some of the larger textbooks because of their size. In therapy, medicine in Scotland would appear to be slightly less advanced than in the U. S., but, in other respects, both modes of practice would seem very similar. Dr. Davidson's work should prove to be an interesting and valuable addition to the still uncrowded field of books on internal medicine.

Therapeutische Technik für die ärztliche Praxis. Herausgegeben von Prof. Dr. Karl Hansen, Lübeck. Unter Mitarbeit von H. Brodersen, et al. Third edition. Cloth. 89 marks. Pp. 986, with 695 illustrations. Georg Thieme, Diemershaldenstrasse 47, (14a) Stuttgart O; agents for U. S. A., Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 1952.

Like many recent works, this volume has been written by several authors, each dealing with the subject with which he is an authority. In format the book leaves nothing to be desired; the paper, type, binding, and illustrations are of the finest quality. In content it is comprehensive, but it is notably deficient in the newer remedies, especially the antibiotic drugs. Penicillin and aureomycin are recommended for treatment of syphilis and gonorrhea, but they are not prescribed for other infections. The book is divided in two sections, general therapy and special therapy. Basic principles and methods in psychotherapy make up the final chapter. Those who use psychotherapy are reminded that the therapist himself should make sure that he is "normal," but no standard by which to measure his fitness is given. This stand is justified, however, in view of the current interest of psychologists and other nonmedical persons in this field.

Our German colleagues have always been excellent physiotherapists, and there are satisfactory chapters on light, heat, and electricity in therapy. Each specialty, such as otorhinolaryngology, is handled well, but there is nothing strictly new. Discussions of radiology and radioactive materials are up-to-date. While the book is comprehensive and detailed, with a review of the old methods and systems, which have the advantage of being tried and proved, the latest advances should have been included. Conservatism is indeed a virtue, but, if treatment is to continue promptly, fully, and completely, we must work by the trial and error procedure on concepts based on recent knowledge.

Nurses Handbook of Obstetrics. By Louise Zabriskie, R.N., Director, Maternity Consultation Service, New York City, and Nicholson J. Eastman, M.D., Professor of Obstetrics in Johns Hopkins University and Obstetrician-in-Chief to Johns Hopkins Hospital, Baltimore. Ninth edition. Cloth. $4.75. Pp. 695, with 377 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; Aldine House, 10-13 Bedford St., London, W.C.2; 2083 Guy St., Montreal, 1952.

This well-known textbook has been thoroughly revised, and the contents have been brought up-to-date. The chapter on prenatal care has been amplified and greater emphasis placed on the normal physiological reactions to pregnancy. The chapter on premature care has been rewritten completely. Student self-examination questions also have been revised and expanded. The format has been changed to double column, with the type size reduced, and some new headings have been introduced to clarify the material. This authoritative textbook by two well-known teachers of obstetrics should continue to occupy a prominent place in nursing education.

Handbook of Diet Therapy. By Dorothea Turner. Written and compiled for American Dietetic Association. Second edition. Cloth. $3.50. Pp. 138. University of Chicago Press, 58th St. and Ellis Ave., Chicago 37, 1952.

This excellent handbook has been extensively revised but retains the same plan of organization and presentation used in the first edition. Therapeutic diets are formulated by a simple, practical, and sound method. A basic plan of food intake for the normal person is outlined and modified to meet the requirements of disease and the needs of the individual patient. Diets are evaluated readily in terms of the nutritive value of each food in the basic regimen. Classification of therapeutic diets in terms of dietetic principles eliminates confusion in terminology and appreciably reduces the number of diets to be considered.

The nutrient content of normal and therapeutic diets has been recalculated, in conformity with the values published recently by the Department of Agriculture. New sections have been written on low-sodium diets and on diets in diabetes mellitus. In the latter section, a simplified method for calculation of diabetic diets is discussed that is based on revised categories of food composition proposed by a joint committee of the American Dietetic Association, the American Diabetic Association, and the United States Public Health Service, Diabetic Section. Tables giving the caloric value and nutrient content of foods have been revised, and tables of the amino acid and sodium content of foods have been added. A chapter on the short method of calculating the nutrient content of diets has been included in the appendix.

This book is well organized, scientifically accurate, and easily understood. It is the most practical book that has appeared in this field and should prove most valuable in teaching diet therapy to nurses, dietitians, and medical students. It should also be useful as a reference for both the dietitian and the practicing physician.

The reviews here published have been prepared by competent authorities and do not represent the opinions of any official bodies unless specifically stated.

QUERIES AND MINOR NOTES

THE LUPUS ERYTHEMATOSUS TEST

TO THE EDITOR:—*Please give complete instructions for the performance of the lupus erythematosus test in which the serum of the suspected patient and white cells from the peripheral blood of a normal subject are used. I would also appreciate references regarding the technique and interpretation of the test.*

M.D., Alabama.

ANSWER.—*The Three Necessary Elements.*—At present there seem to be three elements necessary for the production of the lupus erythematosus cell phenomenon: 1. The L. E. factor, which occurs in the gamma globulin fraction of the plasma of patients with systemic lupus erythematosus, is fundamental for production of the L. E. cell phenomenon. The L. E. factor causes lysis of cell nuclei, as evidenced by swelling, homogenization, and decreased staining reaction of the chromatin in the cells affected. 2. The next requisite for formation of L. E. cells is nuclear material with which the L. E. factor can react. This nuclear material is most commonly derived from the nuclei of the polymorphonuclear leukocytes. Such cells may come from the blood or bone marrow of the patient who has systemic lupus erythematosus, or they may come from the blood or bone marrow of a donor not afflicted with systemic lupus erythematosus. When the L. E. factor and the nuclear material react in the aforementioned lytic process, the resulting homogeneous mass is chemotactic and attractive to phagocytic cells. 3. The third element is a phagocytic cell. The L. E. cell phenomenon is completed when the lysed nuclear mass has been engulfed by a phagocytic cell or cells. The phagocytic cells most commonly observed to be clustered about the lysed nuclear material or the cells which actually have engulfed the material and have become L. E. cells are neutrophilic polymorphonuclear leukocytes. Eosinophilic polymorphonuclear leukocytes may, however, function in the same manner as neutrophilic polymorphonuclear leukocytes. The phagocytic leukocytes may come from the blood or bone marrow of the patient with systemic lupus erythematosus or they may come from the blood or bone marrow of a donor who does not have the disease.

The Secondary Factors.—In demonstrating the L. E. cell phenomenon, there are secondary factors that it is important to consider: 1. The first is time. The L. E. cell phenomenon is an in vitro manifestation and evidently does not occur in vivo, or, if it does, then the process is so limited in activity that this consultant has never demonstrated it by the usual direct blood and bone marrow smear preparations. Blood or bone marrow material must, therefore, be held in vitro sufficiently long for the reactions responsible for the L. E. cell phenomenon to take place. Twenty minutes is probably the minimal time necessary for maximal results, while extension of the time up to two hours may be better, depending on the circumstances. 2. The other secondary factor is coagulation. The production of L. E. cells is greatly accentuated by coagulation, and, while the L. E. cell phenomenon will take place in the presence of anticoagulants, such agents evidently inhibit activity by disturbing the mechanics of coagulation or some other enzyme system.

Techniques.—With knowledge of the foregoing facts about the L. E. cell phenomenon, any number of laboratory techniques can be devised for its demonstration. The following techniques have been used successfully:

1. Patient's Serum Plus Donor's Cells: (*a*) Allow 10 cc. of the suspect patient's blood to coagulate and pipet off the serum for use as the menstruum; (*b*) mix 10 cc. of blood from a healthy donor with a small amount of heparin to prevent coagulation, and centrifuge at 1,800 to 2,000 rpm for about five minutes (this blood may be defibrinated to avoid the use of an anticoagulant); (*c*) pipet off the "buffy coat" or leukocytes, mix with the suspect patient's serum, and allow this mixture to stand at room temperature for 20 to 30 minutes; (*d*) centrifuge the mixture as before and again pipet off the cellular layer; (*e*) centrifuge again the resulting cellular concentrate, in a Wintrobe hematocrit tube if necessary, to obtain a cellular preparation; (*f*) make smears on chemically clean glass slides or coverslips, as is done for usual blood or bone marrow preparations, and stain by the usual technique; (*g*) examine the preparations under an oil immersion objective.

2. Clotted Blood Techniques: These methods are far more sensitive than any this consultant has employed heretofore because of accentuation of the process by coagulation. Another advantage of these procedures is that the suspect patient supplies all necessary elements for producing the L. E. cells and a donor does not have to be employed. On the other hand, great caution must be employed in distinguishing nuclei damaged by the mechanics of the procedure from nuclei lysed by the L. E. factor. However the nuclei are altered, the damaged nuclear material may be engulfed by phagocytic cells (Tart cells) and, if the change is not attributable to lysis, erroneous interpretation will lead to a false positive report.

Clotted Blood Technique 1: (*a*) Put 2 to 4 cc. of venous blood from the suspect patient into a chemically clean centrifuge tube and allow it to coagulate at room temperature for two hours; (*b*) loosen the clot and centrifuge for five minutes at 1,500 rpm; (*c*) discard the pipetted serum; (*d*) break up or repeatedly puncture the clot with a glass rod or wooden applicator sticks; (*e*) fish out and and discard the clot; (*f*) centrifuge the tube as before, and make smears of the sediment for staining.

Clotted Blood Technique 2: (*a*) Withdraw 10 cc. of the suspect patient's blood, place it in a chemically clean centrifuge tube, and allow the blood to stand and to coagulate at room temperature; (*b*) in about two hours, discard the serum, and break up the clot with wooden applicator sticks, or force the clot through a screen (40 wires to the inch), collecting the cellular serum in a Petri dish below; (*c*) centrifuge the resulting serum-cell mixture, and use the resulting cellular layer in making smears for staining and study, as in the other techniques.

Interpretation.—Although free masses of lysed nuclear material, with or without neutrophilic polymorphonuclear leukocytes clustered about them, are very suggestive of the L. E. cell phenomenon and should encourage further search or repeated examinations, a positive diagnosis should not be made without identification of a true L. E. cell. Distinction between the damaged, engulfed lymphocytic nuclei seen in tart cells and the homogeneous, lysed chromatin material seen in L. E. cells is essential if false positive reports are to be avoided.

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any official bodies unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

ULTRAVIOLET LIGHT

To THE EDITOR:—*Are there any harmful effects from the continual use of ultraviolet radiation, e. g., small exposures daily of one or two minutes or a longer exposure at less frequent intervals? Is there any safe distance and time for exposure for a healthy person who does not have any abnormal skin condition or diabetes?*

M.D., Massachusetts.

ANSWER.—It is doubtful that any harm will result from small daily exposures of two minutes or a longer exposure at less frequent intervals provided the intensity of the ultraviolet light striking the subject is not too great. Repeated exposure to ultraviolet rays can cause chronic skin lesions, which may be precancerous, such as keratosis senilis and xeroderma pigmentosum. If the cells of the basal layer of the skin receive an excessive quantity of such radiant energy, the two protective processes of cornification and pigmentation become abnormally great (hyperkeratosis and hyperpigmentation) and another degenerative process starts. Persons lacking in pigment who are much exposed to ultraviolet rays show the highest percentage of skin cancer. The developing neoplasm occurs in the place of greatest proliferation, beginning in a wart-like hyperkeratosis, a precancerous change. A cancer develops from precancerous lesions not only as a result of a continuation of the initial insult but as a result of continued trauma. Thus ultraviolet rays do not cause cancer in themselves. They produce characteristic cell changes leading to precancerous lesions of the skin. Any irritation, including continued and excessive ultraviolet radiation, can cause precancerous lesions to become malignant.

Exposures to the sun should be of durations that produce first a minimum of erythema. When artificial sources of ultraviolet light are used, such as the carbon arc or mercury lamp, it is necessary to determine the minimum erythemal dose of each lamp used. The time of this minimum dose is determined for each lamp operated at a fixed distance from the subject. It is customary to begin ultraviolet exposures with no more than the calculated minimum erythemal dose. Due consideration must be given to the fact that blond skin will burn more readily than brunette skin.

TREATMENT OF RECTAL PROLAPSE

To THE EDITOR:—*What are the modern methods of treatment, including surgical, for prolapse of the rectum in infants, children, and adults?*

Edward W. Sickels, M.D., The Dalles, Ore.

ANSWER.—Rectal prolapse in infants and children is mucosal in almost every instance. Mothers invariably become upset over the sight of prolapsed, congested rectal mucosa. Therefore, the first step in treatment is to allay their fears and assure them that surgical treatment is rarely indicated. The second step is to outline and carefully explain your day to day instructions. Demonstrate to the mother exactly how to replace the protrusion. Wrap toilet paper or kleenex® around the examining finger (for traction); insert the finger into the lumen of protrusion and slowly and methodically ease the mass back into place. Gently withdraw the finger, leaving the paper to disintegrate in the anal canal. The stool should be softened by dietary measures and/or safe, mild medication. Defecation in the recumbent position is helpful. After reducing the prolapse and cleansing, place a small cotton pledget against the anus and strap the buttocks together with adhesive tape. It is advisable to inquire into the toilet habits. Using a child's "toidy" seat is preferable to permitting the child to sit hunched over on the regular seat with the buttocks sagging low in the bowl. The growth of the child will bring increased strength to the anorectal and musculofascial supports, providing a spontaneous cure in most cases.

It is seldom necessary to resort to the submucous injection of sclerosing solutions in the infant, although it may be done as adjunct treatment in stubborn cases. In older children it may be required. The drugs used are either 5% quinine and urea hydrochloride or 5% phenol in pure olive oil. Repeated linear injections are made into the submucosa in each quadrant except the anterior one. The technique and dosage are similar to those used in the treatment of hemorrhoids. If possible, linear cauterization should be avoided in the child.

The treatment of prolapse in the adult must be predicated on the type and severity. Mild, mucosal prolapse has been treated with some success by use of submucous injections of 5% urea hydrochloride, 5% phenol in olive oil, or linear cauterization with actual cautery. Greater success will be attained with surgical treatment. Mild, moderate, or severe mucosal (sometimes called partial) prolapse is most successfully cured with surgical repair. The technique commonly used for removal of large internal hemorrhoids can be applied, i. e., segmental, longitudinal excision of redundant mucosa, utilizing the clamp-excision suture technique. Three or four segments are resected, always in the long axis and always with normal, intact mucosa intervening. Ample drainage adjacent to each wound is essential for smooth, uncomplicated healing. True prolapse, or procidentia involving all layers of the bowel, is in reality a sliding hernia and actually is not common. It is seen most frequently in aged and debilitated persons. Many surgical methods of treatment have been devised using the abdominal or perineal (amputative) approach. No one technique has been uniformly successful. J. E. Dunphy described a combined (*Surg., Gynec. & Obst.* **86**:493, 1948) abdominoperineal procedure offering as good results as any to date.

STERILIZATION OF SURGICAL INSTRUMENTS

To THE EDITOR:—*For years our community hospital has sterilized surgical instruments in metal pans with loosely fitting lids. Disk indicators placed inside the trays indicate complete sterilization. Recently, a new surgical nurse made the statement that, because the lids were on the trays during the autoclaving, the instruments could not be considered sterile. Is there any validity to this nurse's contention?*

M.D., Arizona.

This inquiry was referred to two consultants, whose respective replies follow.—ED.

ANSWER.—This nurse's contention definitely is not valid. For the usual times and temperatures of autoclave sterilization, it is essential that the material to be sterilized be exposed to saturated (wet) steam, and the attainment of a given temperature alone is not sufficient. A loosely fitting lid would not, however, interfere appreciably with the penetration of steam under pressure to displace contained air to reach the conditions required for autoclave sterilization.

ANSWER.—The microbicidal power of steam develops when the steam contacts a colder object and gives up enough latent energy to heat the object to the temperature of the steam. The condensate that results wets the colder object. Two of the three requisites for rapid sterilization, temperature and moisture, are thus present simultaneously. The third factor, period of exposure, varies with the temperature of the steam. Clean, dry, heat-resistant spores are destroyed by 13 minutes' exposure to saturated steam at 250 F (121.1 C) (15 lb. per square inch). Two minutes suffice at 270 F (143.3 C) (27 lb. per square inch). Mechanical contact between moist heat and bacteria is essential. In the case of instruments, with which sterilization is a surface phenomenon, the entire surface must be wet as the instrument is heated. Grease and oil soiling the instruments prevent access to the surface by the steam. Tightly apposed surfaces, as in jaws or catches, may remain dry and, hence, require prolonged exposure for sterilization by dry heat (four hours at 250 F). Hence, instruments must be clean and their locking parts loose for reliable sterilization by steam. Air is trapped in the hospital sterilizer when the door is closed. Because it is denser than steam it pools in upright vessels and at the bottom of the sterilizer, preventing mechanical contact of the lighter steam, which layers on top, with objects to be sterilized. An air ejector at the lowest point of the sterilizer permits the air to spill out. A horizontal path must be provided for lighter steam to displace the heavier air from vessels in the sterilizer so that it can contact, heat, and wet their contents. Lids that fit tightly and the upright position of the vessel interfere with the gravity convection of steam into the vessels and the development of moist heat in the contents. Heating that ultimately occurs owing to conducted or radiated energy is dry, and more prolonged exposure is required than when moist heat is the microbicidal agent. Quantitatively, the prob-

lem of how much steam is necessary for sterilization resolves itself into a problem of the size, shape, and contents of a vessel. It takes the latent energy in 865 cc. of steam to heat a size 6½ rubber glove to sterilizing temperature. One cubic centimeter of moisture is deposited on the surface of the glove as a result of the energy exchange. A shallow tray with a poorly fitted lid might permit this exchange of air and steam reliably. In routine sterilization, however, better control and increased reliability result from the established rule that dry vessels must be placed on their sides to provide a horizontal path for the escape of air.

TESTING THE HEARING OF SCHOOL CHILDREN

To the Editor:—*Is there some simple means of testing the hearing of school and preschool children, one that could be used by a layman? Is the watch-tick test reliable?*

Fred Ben Quincy, M.D., Williamson, W. Va.

Answer.—The best reliable means of testing the hearing of school children is the group audiometric screening test followed by individual audiometric tests of those who fail the screening test. These tests must be made by a trained person, preferably a teacher or school health nurse trained in this procedure. It has been found that the watch-tick, whisper, and spoken voice tests are quite unreliable in detecting cases of moderate hearing loss or hearing loss confined to part of the tone range. Testing the hearing of preschool children is a somewhat different and more difficult problem, since these children may not respond to pure tones and yet have normal hearing. Various special tests have been devised for determining the hearing of infants and young children. Further information on testing the hearing of school and preschool children can be obtained from the Committee on the Conservation of Hearing of the American Academy of Ophthalmology and Otolaryngology, 100 First Avenue Building, Rochester, Minn., or from Dr. Kenneth Nolan, Director for School Health of the City of Chicago, 228 N. LaSalle St., Chicago.

PROCAINE HYDROCHLORIDE FOR SPRAINS

To the Editor:—*It is not an uncommon practice to inject procaine hydrochloride (novocaine®) into recently sprained joints, especially the ankle, to allay pain and to enable athletes to participate in important games. Assuming that no fracture is present, is such a procedure harmful?*

Royal Reynolds, M.D., College Park, Md.

Answer.—In the early thirties, Prof. René Leriche advocated the use of procaine hydrochloride in sprained ankles. He limited its use to simple sprains in which he felt there was no ligamentous or bony damage as evidenced by clinical and roentgen findings. After injection, he prescribed normal use, such as walking. There is no special danger attached to the procedure when it is used in this way. However, it is difficult to say with absolute certainty that there is no ligamentous damage in a mild sprain, and, besides, mild sprains will respond to usual therapy in three or four days. Hence, in treating athletes, it is a safer practice not to rely on the use of procaine, because, if the patient enters abnormal activity like football, there is a great risk of severe damage being done, since the protective symptom, pain, is masked.

WIDAL'S REACTION

To the Editor:—*What is the behavior of Widal's reaction during chloramphenicol treatment of typhoid? Does the reaction become negative directly with the fall of temperature or does the titer decrease gradually?*

Naguib Habib, M.D., Cairo, Egypt.

Answer.—Observations based on a limited number of patients with typhoid treated with chloramphenicol indicate that this drug has little influence on the agglutinin response (Widal's reaction). If treatment is successful and is begun during the first two or three days of illness, somewhat less antibody is produced. As might be expected, the Widal test under these circumstances may become negative somewhat earlier.

THE TWO-STEP TEST

To the Editor:—*In performing the two-step test, why is the level of the S-T segment compared with that of the P-R or P-Q segment, while in routine electrocardiography the S-T segment is considered elevated or depressed in relation to the T-P base line?*

M.D., New York.

Answer.—In electrocardiograms obtained following exercise, the level of the S-T segment is compared with that of the P-R segment for the following reasons: 1. Shortening of the T-P segment associated with increase of rate may result in superposition of P on the descending part of the preceding T; thus, no isoelectric T-P segment can be identified. 2. Appearance, or accentuation, of U waves is common following exercise. This, in association with shortening of the T-P interval, frequently prevents determination of the actual level of the T-P interval. 3. A frequent, though normal, alteration of the electrocardiogram following exercise is the development of a marked T_a wave (auricular repolarization wave). This broad and normally negative deflection may extend into the S-T segment and depress it below the isoelectric line. Such "false" deviations of the S-T segment can, however, be distinguished from abnormal ones by correlating the levels of P-R and S-T segments. A pathological depression of the latter will exceed that of the former, while in the presence of a merely accentuated T_a wave the two segments are at the same subisoelectric level.

HUMIDITY IN THE HOME

To the Editor:—*What is the ideal, healthy humidity for steam-heated apartments and office buildings in Chicago during the winter? What inexpensive, easily installed, approved methods may be used to obtain this desired humidity?*

M.D., Illinois.

Answer.—The American Society of Heating and Ventilating Engineers sets 40% relative humidity at a dry bulb temperature of 73 F as an ideal humidity for winter indoors. In the home, this humidity is difficult to maintain unless the house is well insulated and has storm sashes to prevent condensation on the windows. The comfort range may be varied from the ideal relative humidity either by decreasing the relative humidity and increasing the temperature or by increasing the relative humidity and decreasing the temperature. For example, comfort can be obtained if the relative humidity is 30% and the temperature of the room is 74 F or if the relative humidity is as high as 60% and the temperature is kept at 71 F.

Any humidifying device that increases the relative humidity of the room is a step in the right direction. There are units on the market for home use that can be bought and installed at moderate cost. Those for offices are usually more expensive, depending on the volume of the space involved.

TREATMENT OF YOUNG WOMEN AFTER OVARIECTOMY

To the Editor:—*Should hormone treatment be instituted in young women after complete hysterectomy and bilateral ovariectomy, or should treatment be started only when symptoms appear? What is the consensus on this problem?*

M.D., New York.

Answer.—The opinions on this subject are diverse. The most sensible idea appears to be to treat only those patients in whom symptoms develop that bother the patient considerably. If hot flushes or flashes occur they may last for only a short time until the various glands of internal secretion adjust to the condition. A much more important aspect is the question of whether the woman has enough vaginal atrophy to produce dysparunia, and even this is often completely relieved by a little jelly such as that used to examine patients. Often, low dose vaginal suppositories of estrogenic substances may be used. If use of hormones is advised, the minimum satisfactory dose to relieve symptoms should be used, and they should most certainly be administered orally or vaginally rather than by injection. If estrogens are given, their administration should be stopped periodically to be sure they are still needed.

POSSIBLY NEUROGENIC HYPOGLYCEMIA

TO THE EDITOR:—*A woman, aged 29, gives a history of nervous spells and being very tired if she does not take sugar. In addition to the normal amount, she takes 4 teaspoonfuls of sugar and 3 teaspoonfuls of honey at a meal; if she takes less she feels weak. She requires more sugar if she does hard work. At bedtime, she takes the juice of one orange with 2 teaspoonfuls of sugar. Her blood sugar level is 90 mg. per 100 cc. Results of a glucose tolerance test were as follows: in a fasting state the blood sugar level was 98 mg. per 100 cc. and the urine was negative for sugar; after one-half hour, blood sugar level 163 mg. per 100 cc., and urine negative; after one hour, blood sugar level 180 mg. per 100 cc., and urine 2+; after one and one-half hours, blood sugar level 125 mg. per 100 cc., and urine 1+; after two hours, blood sugar level 135 mg. per 100 cc., and urine negative; after three hours, blood sugar level 96 mg. per 100 cc., and urine negative. I should like suggestions on diagnosis and treatment.* *Joel L. E. Peterson, M.D., St. Paul.*

ANSWER.—It would be well to know whether there is a positive diabetic heredity, what is the present weight of the patient and whether she is gaining or losing weight, what is the basal metabolic rate, and what is the composition of the total diet for an entire 24 hour period, including the added sugar, honey, and orange juice, which alone provide daily 100 to 125 gm. of carbohydrate. Certainly one should defer diagnosis, even between "unclassified glycosuria" and diabetes, the latter because it would rest only on glycosuria, the peak blood sugar value of 180 mg., and the two hour value of 135 mg. The presence of an islet cell tumor of the pancreas is unlikely but could be excluded more definitely by a blood sugar determination after more prolonged fasting or by extending the sugar tolerance test to four, five, and six hours after the ingestion of 100 gm. of glucose. True renal glycosuria is excluded by the lack of evidence of significant lowering of the renal threshold of sugar.

Because of the character of the symptoms, so-called neurogenic hypoglycemia is a definite possibility, although not well substantiated by the results of the glucose tolerance test. Here, too, it would be helpful to carry out the test for six hours to ascertain whether significant hypoglycemia occurs. Treatment of this condition consists of reassurance, easing of nervous tension, and the regular use of atropine or belladonna with small doses of phenobarbital. The diet should be adequate in vitamins and minerals, moderately restricted in carbohydrate (150 to 200 gm. daily), liberal in protein, and adjusted in fat according to the body weight. Small forenoon, afternoon, and bedtime feedings should be taken regularly; these also should be restricted in carbohydrate and liberal in protein. Within a month, the glucose tolerance test in extended form should be repeated. For three days prior to such a test, dietary restrictions should be waived and an unrestricted carbohydrate intake allowed. Then a reevaluation of the situation should be made on the basis of a comparison of these results with those obtained previously and the patient's response to the program outlined, taking into account the factors mentioned at the beginning of this answer.

CREEPING ERUPTION

TO THE EDITOR:—*A woman who spent the summer in Florida has irregular erythematous lesions in the antecubital fossa and on the index finger that are linear and slightly raised, and they itch. Spraying with ethyl chloride changes the course but does not cure the lesions. The patient has been told that it is a worm in the skin. I can find no data on it.*

J. J. Blue, M.D., Cedarville, Mich.

ANSWER.—The woman probably has larva migrans (creeping eruption). An effective treatment is to freeze the parasite at the advancing end either with solid carbon dioxide to the point of producing a superficial blister or with ethyl chloride to the point of producing a board-like hardness. Treatment with stibophen (fuadin®) and other methods of treatment are mentioned in all standard textbooks of dermatology.

EPIDERMOLYSIS BULLOSA

TO THE EDITOR:—*A 20-year-old girl has, since childhood, had recurrent blisters on parts of her body that are exposed to some kind of pressure. They occur more commonly on her feet and hands, but a tightly fitting brassiere occasionally causes some elongated blisters on her chest. All blisters arise without previous itching on apparently healthy skin. Their size never exceeds that of a quarter, and they are filled with a serous fluid. The patient used to open these blisters herself with a needle, and while secondary infections have been rare, she once had erysipelas. There is a definite hereditary trend apparent, which can be traced back over three generations, with no preference in regard to sex. Physical and laboratory examinations show normal results. Is epidermolysis bullosa the correct diagnosis, and what treatment is recommended?*

M.D., West Virginia.

ANSWER.—Epidermolysis bullosa is the most likely diagnosis. Unfortunately, there is no effective treatment for the condition other than the use of measures to avoid trauma and, when necessary, rational therapy of traumatized or infected lesions.

CONTACT LENSES

TO THE EDITOR:—*Local opticians make far-reaching claims to the effect that contact lenses in nearsighted children will prevent progression of nearsightedness, that contact lenses will take care of presbyopia to a certain degree, and that after a cataract operation a patient can use the contact glass alone for both distance and close viewing. Is there any truth in this?*

M.D., Illinois.

ANSWER.—There is no evidence that wearing of either contact lenses or ordinary spectacles prevents progression of nearsightedness, which in the ordinary form is an inherent growth phenomenon, any more than putting a brick on the head of a baby will prevent its growing. There is no evidence that contact lenses will retard the onset of presbyopia. It occasionally happens that an aphakic patient can see in the distance and also read to some extent with his ordinary cataract glasses. These are rare cases, and it is possible that somewhat the same condition could occur with a contact glass, although it is less likely to happen because the vertex distance is fixed in the latter case.

SALIVA OF THE VAMPIRE BAT

TO THE EDITOR:—*Blood runs freely from the wound produced by the vampire bat, and the bat laps it up instead of sucking it. It is believed that the blood does not clot because the bat's saliva has an anticoagulant effect. Has an effort been made to apply the saliva of the vampire bat in anticoagulant therapy?*

Samuel Barmak, M.D., Pinewald, N. J.

ANSWER.—Extracts of the salivary glands of a vampire bat of Brazil (Desmodus rufus) were reported by Bier (*Compt. rend. Soc. de biol.* **110**:129, 1932) to have both a fibrinolytic and a direct anticoagulant action. This work antedated all modern methods for the study of coagulation; however, control tests on non-blood-eating bats gave negative results. No reports have been published of attempts to employ the saliva of the vampire bat in anticoagulant therapy. The reported prevalence of rabies in this animal would be one of many difficulties encountered in utilizing such an exotic source material.

DERMATITIS FROM JEWELRY

TO THE EDITOR:—*A patient gets contact dermatitis every time she wears earrings; if she wears them for half a day the lobes of her ears become swollen, and it takes three to four days for the swelling and itching to disappear. She cannot wear rings for the same reason. Is there any solution with which the rings or earrings could be painted to prevent this condition?* *John T. Kaye, M.D., Menominee, Mich.*

ANSWER.—The sensible course would be not to wear the earrings, but if this woman feels she must wear them to a particular social affair, painting the contact surface with flexible collodion or colorless nail lacquer should afford protection for a short period.

THE FREI TEST AND THE INGUINAL BUBO

TO THE EDITOR:—*I am frequently confronted with the problem of differential diagnosis of the inguinal bubo. I have yet to see a positive reaction to the Frei test. 1. How long after exposure does the Frei test become positive, i. e., is the skin test useful in the diagnosis of the acute disease or only the chronic complications? 2. Will a skin test, whether the results are negative or positive, give sufficient stimulation to cause a significant complement fixation? 3. If the answer to question 2 is in the affirmative will a negative Frei test ever give rise to a subsequent positive test? Will this phenomenon occur with any type of cutaneous testing?*

Donald A. Fusia Jr., M.D., San Francisco, Calif.

ANSWER.—1. The Frei test becomes positive about three to four weeks after the first clinical manifestations of lymphogranuloma venereum appear and thereafter, in the absence of effective treatment, remains positive for the remainder of the patient's life. The interpretation of a positive Frei test is, therefore, one of considerable difficulty. Unless the patient shows clinical manifestations reasonably characteristic of lymphogranuloma, the positive Frei test may serve only to confuse the diagnostic picture, since it may mean only that the patient has been infected with lymphogranuloma in the past, although his presenting complaints have nothing to do with the disease. 2. A skin test will not give sufficient stimulation to cause complement fixation. 3. The performance of a Frei test with negative results will not lead to a subsequent positive skin test. This phenomenon does not usually occur with any type of cutaneous testing but may occasionally occur in skin testing with Brucella antigens (brucellin or brucellergen®).

URTICARIA FOLLOWING TETANUS TOXOID

TO THE EDITOR:—*I have read the question raised by Dr. Walter E. Fleischer and commented on in* THE JOURNAL, *Jan. 24, 1953, page 345, regarding "Urticaria Following Tetanus Toxoid." May I take the liberty of making a few dissenting remarks? There is a distinct possibility that the patient in question may have a serious generalized reaction the next time that he is inoculated with any kind of tetanus toxoid, even in small quantities. Therefore, it would appear wise to recommend extreme caution in subsequent procedures on this patient involving the use of this agent. Should there be any indication in the future to use tetanus toxoid on this patient, a skin test with fluid toxoid diluted 1:100 or higher presumably would be safe, provided epinephrine or aminophylline was at hand in case of a severe reaction. Before undertaking additional immunization, however, it would be desirable to find out from drug firms whether it is possible to obtain a toxoid that is not produced on a potentially allergenic medium, since it is conceivable that this patient is sensitive to a constituent of the medium rather than to the toxoid itself.*

Some explanation is indicated for the fact that the patient has received eight injections of tetanus toxoid. It is now an almost universal practice to give an adequate basic immunization (two initial doses of precipitated toxoid or three doses of fluid toxoid plus an additional dose at an interval of six months to one year) and then to give single booster doses at about four year intervals. Since this patient was immunized in 1944 and received six additional doses in 1948 and two additional doses in 1952, it is likely that he will be well protected against tetanus for the next decade. To play safe, reimmunization could be considered in his case in four or five years. Prior to administering the single booster dose that would ordinarily then be indicated, the foregoing precautions should be observed. It might also be wise to try to obviate the need for additional immunization by sending a sample of the patient's blood to a laboratory capable of titrating its antitoxin content. The antitoxin titer at that time will almost certainly be over 1 unit, unless the patient has some unusual defect in antibody formation.

Regarding the question of testing for sensitivity, it would appear undesirable to use the term "sensitivity test (Moloney) for alum-precipitated toxoid" for two reasons: 1. The Moloney test, analogous to the tuberculin test, is designed to detect sensitivity of the delayed allergic type, manifested as induration and erythema 12 to 24 hours after the test and lasting four to seven days or longer. Most persons familiar with the use of this test are aware that it induces a reaction different from the urticarial response described in this patient. Although diluted toxoid would undoubtedly induce urticaria in this patient, it would appear preferable to use some other term than the "Moloney test" for the procedure in this case. 2. I know of no basis for making a distinction between sensitivity to alum-precipitated toxoid and that to fluid toxoid. Furthermore, if the patient should be sensitive to tetanus toxoid or the ingredients in which it is suspended, fluid toxoid might be somewhat more hazardous to use than precipitated toxoid, since the fluid materials would be more rapidly absorbed.

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CONGENITAL METHEMOGLOBINEMIA

TO THE EDITOR:—*In* THE JOURNAL, *Dec. 6, 1952, page 1443, in Queries and Minor Notes under the title "Congenital Heart Disease" is a letter from M.D., Brazil, requesting an explanation for three consecutive sons born with congenital cardiac anomalies. Apparently, the only criterion used in formulating the diagnosis of congenital cardiac anomalies was that the patients are blue. There is a distinct possibility that one or all three of these children have congenital methemoglobinemia. This condition produces cyanosis and is frequently confused with congenital heart disease. If the condition exists untreated over many years, right ventricular hypertrophy, dilatation of the pulmonary conus, and pulmonic murmurs may develop, thus strengthening the examiner's impression of congenital heart disease. To establish or to rule out this possibility a careful family history should be taken to detect other cyanotic relatives. The blood should be examined in a spectrograph and in a spectrophotometer for qualitative and quantitative evidence of methemoglobin. Patients with this disease lack an enzyme system in their red blood cells for converting methemoglobin back to normal hemoglobin and, without treatment, become stabilized at a level of about 40% methemoglobin. Compensatory polycythemia also develops: If methemoglobin is found, acquired methemoglobin from drugs and nitrates in well water must be ruled out. If the inquiring physician lacks access to a spectrophotometer, a therapeutic trial with methylene blue will abolish the cyanosis in a few hours if it is due to methemoglobin. If a diagnosis of congenital methemoglobinemia is established in these patients, the level of circulating methemoglobin can be reduced to almost normal levels and the cyanosis abolished with large doses of vitamin C taken daily in divided doses.*

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HERNIA IN AN INFANT

TO THE EDITOR:—*I would like to comment on the Query "Hernia in an Infant," and the removal of the appendix at time of herniorrhaphy, in* THE JOURNAL, *Jan. 24, 1953, page 345. Surely, every physician with moderate experience has found that acute appendicitis, with the increase of abdominal fluids and slight abdominal distention, frequently opens the inactive sac of a hernia. No right-sided hernia repair, except in the rarest instances, should be done without removal of the appendix, even though two incisions would have to be made, which seldom is necessary.*

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